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TREATMENT OF RHINORRHEA AND OTORRHEA

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In rhinorrhea and otorrhea the cerebrospinal fluid is discharged from the nose and the ear respectively. Both conditions are due to a fistula connecting the cerebrospinal spaces—either the subarachnoid spaces or the ventricular system—with the exterior. Pneumocephalus (air in the cranial chamber) is frequently but not necessarily in association. If the fistula is large enough, air enters the cranial chamber as the fluid passes out. When there is a ball valve arrangement in the fistulous tract, coughing and sneezing may force large quantities of air into the cranial chamber, and if the frontal lobes are pierced a steadily enlarging air-filled cavity in a frontal lobe gradually erodes its way into a lateral ventricle, and the entire ventricular system together with the subarachnoid spaces is then filled with air; this is the terminal stage. The surgical attack on rhinorrhea and otorrhea, however, is precisely the same, for both are due to the same underlying cause, a fistula; closure of this cures both.

The two great causes of rhinorrhea and otorrhea are (1) fractures of the skull and (2) openings created by operative procedures. Less frequent causes are (3) erosions by tumors or infections and (4) congenital abnormalities. Fortunately many fistulas heal spontaneously. Spontaneous healing occurs particularly in otorrhea following fractures of the petrous portion of the temporal bone and is due to the relatively long course of the channel through the petrous bone and the relatively greater thickness of the soft tissues. Post-traumatic otorrhea will usually stop in less than two weeks, and frequently in a day or two. There is therefore no indication for operative intervention for otorrhea of such short duration; this is fortunate, because it would be difficult to determine the site of the fistula, i. e. whether it was in the middle or the posterior cranial fossa. Post-traumatic or postoperative fistulas into the frontal or ethmoid sinuses or fistulas created by operations on the mastoid are frequently slow to heal and may never heal, or they may close and periodically reopen. The explanation is that the drainage tract is usually larger and the soft tissues relatively thin, being only mucosal lining. Usually the fistula persists too long to await nature's efforts at closure by granulation tissue.

A cerebrospinal fistula is always a potential source of meningitis or cerebral abscess, and if the draining fluid persists long enough several attacks of meningitis may occur, and eventually one will be fatal. Many years may indeed elapse before death, or it may come quickly—depending on the chance of infection within the paranasal or mastoid sinuses. Sulfonamide drugs and penicillin are helpful and may prolong life, but the danger of a fatal termination is always present nevertheless. The high percentage of recoveries from meningitis in the presence of cerebrospinal fistulas is due to the continuous drainage afforded by the opening.

It is my strong feeling that a fistula (except those following injury to the petrous bone) should never be left open longer than two weeks unless the fluid is unmistakably diminishing. Closure is now a comparatively simple, danger-free procedure and leaves nothing to chance. The only exception to this statement is closure in the presence of a known, well developed intracranial infection. In 1 of my cases (case 2) organisms were isolated from the fluid but there was no purulent meningitis. In case 8 a cerebral abscess became full blown three weeks after the fistula was closed, but it was certainly there before the operation; at least nothing was lost in the attempt, and had it been closed earlier the abscess would never have developed.

Plum [1] (1931) reported a fistula of eighteen years' duration; Fribourg-Blanc, Lassalle and Germain [2] (1934), one of seventeen years' duration, with intermittent closure for short periods. Wurster [3] (1937) reported one of six and a half

1. Plum, F. A.: Cerebrospinal Rhinorrhea, Arch. Otolaryng. **13**:84 (Jan.) 1931.

2. Fribourg-Blanc, Lassalle and Germain: Deux observations de pneumatocèle intracranienne, Rev. neurol. **2**:51, 1934.

(Footnotes continued on next page)

years' duration; it finally healed spontaneously and had remained closed three years at the time of his report. Thomson reported on this condition [4] (1899) in a patient, which had persisted several years. A number of spontaneous cures are recorded in the literature, but there are many more fatalities.

LOCALIZATION OF THE BONY AND DURAL OPENINGS

When rhinorrhea follows operative procedures, the site of the fistula is along the path of the operative attack and is therefore usually not difficult to find. If the fistula follows a depressed fracture of the skull the depression may indicate its position. But if there is no depression roentgenograms of the frontal region (frontal, ethmoid and sphenoid sinuses) are all important. Even then its location may be in doubt. Drainage of fluid from one nostril predominantly is fair evidence that the fistula is on the corresponding side of the anterior fossa, but that is by no means dependable proof. Cairns [5] (1937) found the opening on the contralateral side; it was explained by a blood clot which filled the other nostril. Then, too, one of the frontal sinuses may be closed for other reasons. There are times when only an exploratory operation will determine the site of the opening. Moreover, there may be bilateral fistulas (Cairns,[5] Adson,[6] Eden,[7] Campbell, Howard and Weary [8]).

To differentiate between a fistula of the frontal and one of the ethmoid sinus may at times be difficult. It is my impression that the differential diagnosis can often be made by observing the cerebrospinal outflow, i. e., if when the head is tilted forward there is a sudden increase in the volume of fluid, it is apparent that the fluid has been contained in a reservoir and is pouring over the edge and that the fistula is located in a frontal sinus. And if the flow of fluid is not altered by tilting the head, an opening in the ethmoid or in the sphenoid cells is indicated.

In 1 case (case 10) I was not able to find the opening in the bone through which fluid poured into the middle ear and thence down the eustachian tube and the pharynx and when the patient was lying down from the nose. The opening into the middle ear was found, but its closure was unsuccessful.

If there is any difference of opinion concerning the advisability of operation for cerebrospinal fistulas, it can be only in those few cases in which the site or side of the fistula cannot be determined beforehand, but even in such unusual cases bilateral exposure is preferable to the almost certain fatality that lies ahead.

METHODS OF SURGICAL CLOSURE OF THE FISTULA

The first successful treatment of rhinorrhea was reported by me in 1926.[9] Autogenous grafts of fascia lata were sutured over the dural opening behind a depressed fracture of the orbit and the frontal sinus. Before this Grant [10] (1923) had attempted to close an opening through a cranial exposure but was not successful, and Teachenor [11] (1923) debated whether to uncover a frontal fistula in order to close the dura. Cushing [12] (1927) reported successful treatment in 3 cases in which rhinorrhea followed removal of orbitoethmoid osteomas; in each a piece of fascia lata was laid over the dural defect. Prior to these cures, 2 patients with similar conditions had died of infection; it was these deaths that prompted the closure with fascia. Rand [13] (1930), McKinney [14] (1932), Cairns [5] (1937), Gissane and Rank [15] (1940), Eden [7] (1942) and Campbell, Howard and Weary [8] (1942) have since reported cures by the use of fascial transplants. The fascia may be taken from the thigh

3. Wurster, H. C.: Cerebrospinal Rhinorrhea: Report of an Unusual Case, J. Indiana M. A. **30**:199, 1937.

4. Thomson, St. C.: The Cerebrospinal Fluid: Its Spontaneous Escape from the Nose, London, Cassell & Co., 1899.

5. Cairns, H.: Injuries of the Frontal and Ethmoidal Sinuses with Special Reference to Cerebrospinal Rhinorrhoea and Aeroceles, J. Laryng. & Otol. **52**:589, 1937.

6. Adson, A. W.: Cerebrospinal Rhinorrhea, Ann. Surg. **114**:697, 1941.

7. Eden, K. C.: Traumatic Cerebrospinal Rhinorrhoea, Brit. J. Surg. **29**:299, 1942.

8. Campbell, E.; Howard, W. P., and Weary, W. B.: Gunshot Wounds of the Brain, Arch. Surg. **44**: 789 (May) 1942.

9. Dandy, W. E.: Pneumocephalus, Arch. Surg. **12**:949 (May) 1926; Pneumocephalus, in Lewis, D.: System of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1943, vol. 14, pp. 311-319.

10. Grant, F. C.: Intracranial Aerocele Following a Fracture of the Skull, Surg., Gynec. & Obst. **36**:251, 1923.

11. Teachenor, F. R.: Pneumoventricle of the Cerebrum Following Fracture of the Skull, Ann. Surg. **78**: 561, 1923.

12. Cushing, H.: Experiences with Orbito-Ethmoidal Osteomata Having Intracranial Complications, Surg., Gynec. & Obst. **44**:721, 1927.

13. Rand, C. W.: Traumatic Pneumocephalus: Report of Eight Cases, Arch. Surg. **20**:935 (June) 1930.

14. McKinney, R.: Traumatic Pneumocephalon, Ann. Otol., Rhin. & Laryng. **41**:597, 1932.

15. Gissane, W., and Rank, B. K.: Post-Traumatic Cerebrospinal Rhinorrhoea with Case Report, Brit. J. Surg. **27**:717, 1940.

or from the covering of the temporal muscle. The fascia may be sutured in place or when this is not practical laid over the defect.

To cure rhinorrhea or otorrhea, it is not necessary that both the opening in the bone and that in the dura be closed. The closure of either will cure the condition. On the whole, closure of the dura is preferable. In 2 of the cases in this series (cases 4 and 5) the bone was waxed (1934 and 1937). This method of closing the defect in the bone was reported by Graham[16] (1937) and later by Adson[6] (1941).

Packing the wound with iodoform gauze was advocated by Peet[17] (1928) and has been used by Gurdjian and Webster[18] (1944). However, packing of the wound is now rarely done, most wounds being closed without drainage.

TREATMENT OF FISTULAS FOLLOWING CRANIAL OPERATIONS

As previously noted, when rhinorrhea develops after a cranial operative procedure the site of the fistula is evident or nearly so. In frontal craniotomy an unusually large frontal sinus may be opened. This is such a potential risk that surgeons should always know from roentgenograms the size of the frontal sinus, and when a low frontal approach is required entry into the sinus can be avoided by correspondingly shifting the bony incision. There are times when entry cannot be avoided, as for example in attacking tumors that invade the frontal sinus. When a frontal sinus is opened a flap of dura can be reflected over the opening and tightly sutured to the overlying galea. If the opening is disclosed by rhinorrhea after the operation is completed the wound should be reopened immediately and this procedure carried out (case 3). During cerebellar operations for trigeminal neuralgia, Ménière's disease, tumor of the acoustic nerve and other conditions a mastoid cell is occasionally opened; the dura should be immediately sutured over it to prevent immediate or subsequent infection.

In another case (case 4) rhinorrhea followed a frontal craniotomy in which the frontal sinus was not opened but in which the dura had been accidentally stripped from the floor of the anterior fossa. Reexploration revealed an opening as large as a slate pencil into an ethmoid cell, and in the opening was an old elevated fracture (of many years' duration). This was plugged with bone wax (1934); there was no corresponding dural opening. The fluid had escaped through the dural suture line, thereby gaining access to the subdural space, where it entered the defect in the bone.

In another case (case 5) an opening in the ethmoid cell was made when the orbital roof was rongeured away in preparation for the removal of an orbital tumor. This opening was waxed later in the day and the dura reflected over it and sutured in place. As a precaution against the possibility of such an accident in operations on orbital tumors, the dura covering the orbital roof is now always reflected mesially; it can then be used to cover any opening in the ethmoid cells.

Nasal operations in which the cribriform plate is punctured and operations in which hypophysial tumors are attacked by the nasal route are other sources of rhinorrhea. Neither of these was encountered in this series.

OTORRHEA FOLLOWING OPERATIONS ON THE MASTOID

There are 4 cases in this series in which otorrhea followed operation on the mastoid; in each case it was due to the operator's chiseling through the mastoid bone and the dura. In 3 of the cases the bony defect was in the roof of the petrous bone about 2 cm. inside the lateral wall of the skull; this is probably the most common site. According to the law of probability, therefore, this is the logical place to look for the fistula. The corresponding dural defect can be sutured and if necessary reenforced by a piece of fascia lata or more conveniently by a layer of the sheath of the temporal muscle. The latter serves just as well as fascia lata for this purpose and is immediately available in the operative area. If the dural defect is near the surface the fascia is sutured in place; if it is too deep it can be laid over the suture line and treated with 3.5 per cent solution of iodine to promote adhesions. It was possible to suture in all of these cases. In a fourth case the dural opening was just back of the mastoid bone. This opening was sutured and covered by fascia, which was merely laid over the suture line and treated with iodine solution; the dura was too thin to support additional sutures. It is evident that an attempt to find the fistula by reexploring the original

16. Graham, T. O.: Cerebrospinal Rhinorrhoea, J. Laryng. & Otol. **52**:344, 1937.

17. Peet, M. M.: Symptoms, Diagnosis and Treatment of Acute Cranial and Intracranial Injuries, New York State J. Med. **28**:555, 1928.

18. Gurdjian, E. S., and Webster, J. E.: Surgical Management of Compound Depressed Fracture of Frontal Sinus, Cerebrospinal Rhinorrhea and Pneumocephalus, Arch. Otolaryng. **39**:287 (April) 1944.

wound of the mastoid would be unproductive, because nothing could be done to the dural opening unless a large area of bone were removed. The incision, therefore, is made anterior to the old incision, so that the roof of the petrous bone can be exposed and the overlying dural defect reached with adequate room for closure; the attack is entirely extradural.

In case 10 a postoperative fistula was found in an unusual site. After the removal of a tumor of the acoustic nerve (by me) that had deeply eroded the petrous bone, it was discovered that a fistula opened into the middle ear and that the fluid was discharged into the pharynx. The tumor had eroded the posterior wall of the middle ear. Since rhinorrhea was an immediate postoperative sequel, the fluid had to come from this site. The ear drum bulged almost to the point of rupture, and after two unsuccessful attempts to find the fistula it was disclosed by injecting methylthionine chloride (methylene blue) (Dr. John Baylor's idea) through the drum with a tiny needle; the walls of the fistula were then colored by the dye. But an attempt to close it with sutures and a fascial transplant was unsuccessful. It would not have been possible to suture a dural graft over the large defect intracranially, but an attempt was made to wax the bed from which the tumor had been extirpated. Perhaps a more careful plastic operation with fascia would now bring results. This is the only case in the series in which there was failure to close a fistula. The patient subsequently died of meningitis; the rhinorrhea persisted one year after removal of the tumor.

RHINORRHEA AND PNEUMOCEPHALUS FOLLOWING DEPRESSED FRACTURES OF THE FRONTAL SINUS

A depressed fracture of the frontal sinus is frequently visible or palpable. In 2 of the cases in this series (cases 1 and 2) it was necessary only to elevate the depressed fragment and remove it temporarily to close the opening in the dura with a fascial transplant. If there is not an adequate exposed area of dura, an additional amount of the inner table of the frontal sinus must be rongeured away until the desired exposure is obtained. The elevated or removed fragment of bone can then be replaced in its proper position and will usually hold without wiring. Without the existence of a depressed fracture a lateral cranial exposure would be preferable to removing the walls of the frontal sinus.

In these cases (1 and 2) both patients had pneumocephalus, with a large frontal defect and ventricular filling. Both were unconscious at the time of admission to the hospital and both recovered. There were no other cases of pneumocephalus in the series.

RHINORRHEA FOLLOWING NONDEPRESSED FRACTURES OF THE FRONTAL AND ETHMOID SINUSES

Fractures of the frontal sinus need not of course be depressed. A linear fracture will tear the underlying dura and cause rhinorrhea. With such a lesion roentgenograms are essential to determine whether the tear is on the right, the left or at times both sides and to differentiate between a crack in the frontal and the ethmoid sinus. To locate the fracture and to disclose intracranial air are important functions of roentgenography in this field.

For revealing a fistula resulting from a nondepressed fracture an intracranial exposure is almost essential and provides a much better cosmetic result. To rongeur away both walls of a frontal sinus in order to expose and close a fistula beneath, as advocated by Teachenor [19] (1923 and 1927), would produce an unsightly deformity. A cranioplasty leaves no deformity, and the incision is entirely under the hair line. My choice of operative attack is a small bone flap, such as is used for hypophysial tumors, with a concealed incision. Whether or not the dura is opened depends on the amount of room necessary to close and reenforce the opening with fascia. With careful closure of the dura the opening in the bone need not be closed, though covering it with bone wax adds safety if the opening is small. Coleman [20] (1937) has used this method of attack. It was first tried by Grant [10] (1923) in probably the first operative attempt to cure pneumocephalus, but the operation was unsuccessful because of uncontrollable bleeding.

Adson [6] (1941) reported 6 cases in which rhinorrhea was cured and advocated a bilateral frontal approach with a coronal incision. Because of troublesome bleeding he routinely ligated the longitudinal sinus, at times both before and after. He reasoned that: (1) he could be sure of finding the fistula on either side (when the side was unknown) or on both sides (when bilateral); (2) better elevation of the meninges was possible because of added room, and therefore (3) better invagination of the edges of the dural fistula was

19. Teachenor, F. R.: Intracranial Complications of Fracture of Skull Involving Frontal Sinus, J. A. M. A. **88**:987 (March 26) 1927; footnote 11.

20. Coleman, C. C.: Fracture of the Skull Involving the Paranasal Sinuses and Mastoids, J. A. M. A. **109**: 1613 (Nov. 13) 1937.

possible during suturation. This is an extensive procedure, and ligation of a longitudinal sinus is a serious addition to it. Moreover, such a wide bone flap broken at the anterior border of the skull must lend itself to opening both frontal sinuses—a complication that every effort should be made to avoid. Cairns [5] (1937) made an enlarged unilateral exposure that was carried some distance across the midline, so as to include much of the other frontal lobe. I should much prefer two separate unilateral flaps (two operations) if bilateral fistulas are present (as in case 11) or even if the side of the fistula is not known (this is only occasionally uncertain). It is usually possible to get adequate exposure by an extradural unilateral approach, and if it is not possible opening the dura and evacuating the cisterna chiasmatis will provide more room than is necessary.

TREATMENT OF OPENINGS IN THE ETHMOID SINUSES

Openings in the ethmoid cells are somewhat more difficult to expose and require the small anterior bone flap just described; it may or may not be necessary to open the dura. If the dura is stripped from the anterior fossa, the opening in the bone may be waxed and a piece of temporal fascia laid over it. Treatment of the fascia with 3.5 per cent solution of iodine will promote adhesions. At this depth and with a thin, easily tearable dura, suturing is difficult or impossible. German [21] (1944) reported 5 cases in which a flap of dura was turned down from the falx cerebri and the crista galli and thrown across the dural defect. Gurdjian and Webster [18] (1944) reported a case in which this procedure was used. For this procedure the dura must of course be widely opened, as in any cranioplastic procedure.

REPORT OF CASES

CASE 1.—*Post-traumatic fistula with a ball valve arrangement into the right frontal sinus.*

T. S., a white man aged 70, was seen on Feb. 20, 1925. There had been an intermittent discharge of watery fluid from the nose since an automobile accident forty-five days before. He was semicomatose on admission to the hospital. His pulse rate was 50 and his temperature was 99.8 F. The white cell count was 8,000. Operation for presumed subdural hematoma was done forty-five days after his injury; pneumocephalus was encountered; air spurted and the brain collapsed when the thin cortex was incised. An opening in the dura and the frontal sinus was disclosed when the frontal lobe was retracted. After the wound was closed the depressed fracture was elevated and the dural defect repaired with a transplant of fascia lata, which was sutured. Entrance of air into the cranial chamber had been by a ball valve arrangement of the fistulous tract; the dural opening was not superimposed on the break in the bone. Air, therefore, could be blown into the brain by coughing and sneezing, but the increased intracranial pressure forced the dura against an intact bony surface and prevented escape of the air. Roentgenograms taken before the cranial operation showed large ventricles and a large frontal defect completely filled with air, but because of his condition I had not waited to inspect them.

Subsequent Course.—Recovery was uneventful; the pneumocephalus immediately cleared.

This case was presented in an earlier publication and was the first in which a fistula causing rhinorrhea and pneumocephalus was cured by fascial repair of the opening (fig. 1).

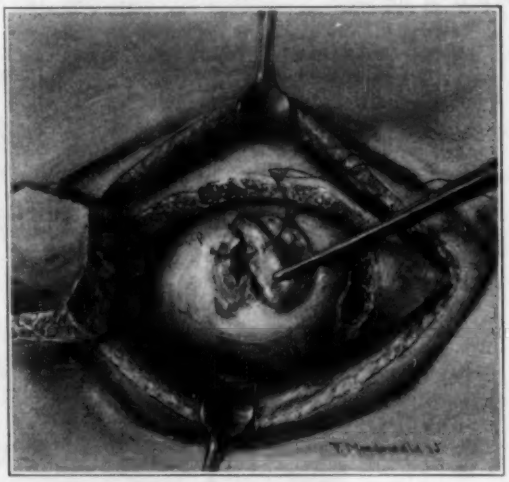

Fig. 1 (case 1).—Drawing showing a facial transplant sutured over the dural defect beneath a depressed fracture in the supraorbital region. It will be noted that the dural opening is not in line with the opening in the frontal sinus. This is a ball valve channel. The air is blown through the dural opening, and the intracranial pressure then forces the dura against the bone and prevents its exit. The air destroyed the right frontal lobe and then burst into the ventricular system, producing total pneumocephalus.

CASE 2.—*Post-traumatic fistula into the left frontal sinus with pneumocephalus and ventricular filling (fig. 2 A).*

W. F., a white man aged 20, was seen on Nov. 23, 1928. The patient was comatose when admitted to the hospital. There was a constant drip of clear fluid from the nose. Two months previously he had been in an automobile accident, after which he was unconscious for two days and then irrational for several days. When he got out of bed rhinorrhea was observed from the left nostril and had since persisted.

On admission to the hospital his temperature was 105 F.; the spinal fluid was xanthochromic and contained 20,700 cells; the white cell count was 17,000. Streptococci were grown from the spinal fluid, but the fluid was not purulent. When his head was tipped forward a half-cup of fluid rolled out.

21. German, W. J.: Cerebrospinal Rhinorrhoea—Surgical Repair, J. Neurosurg. **1**:60, 1944.

Roentgenograms showed the lateral ventricles filled with air and a large air-filled defect of the left frontal lobe. A depressed fracture of the left frontal bone and a crack in the right frontal sinus were disclosed. There was complete paralysis of the left oculomotor nerve.

Operation was performed on Nov. 24, 1928. The old depressed fracture of the left frontal bone was elevated. The incision was made along the supraorbital ridge. An opening 2 cm. long and 1 cm. wide was disclosed beneath it; air escaped. A piece of fascia lata was sutured over the opening and the fragment of bone replaced.

Subsequent Course.—Recovery was uneventful and the rhinorrhea did not recur (fig. 2 *B*). Meningitis did not develop. The patient is now serving with the marines in the South Pacific.

CASE 3.—*Postoperative defect in a frontal sinus.*

T. L., a white man aged 58, was seen on Jan. 26, 1940. Immediately after removal of an enormous osteosarcoma of the skull, rhinorrhea appeared (fig. 3). At the time of operation the opening in the frontal sinus was not observed. On the following day the wound was reopened, and a pedicled flap of dura was reflected over the opening and snugly sutured to the galea. The rhinorrhea immediately ceased; recovery was uneventful.

CASE 4.—*Post-traumatic and postoperative opening into ethmoid cells.*

E. L., a white woman aged 26, was seen on Aug. 25, 1934. A glioma was removed with a section of the left frontal lobe. During the operation an assistant jerked the dura, stripping it from the anterior fossa. Rhinorrhea immediately followed the operation.

On the following day the wound was reopened, and an old elevated fracture lying in an opening in the cribriform plate was disclosed (fig. 4). The upturned fragment of bone left an opening as large as a slate pencil into an ethmoid cell. It was covered with wax. The dura was intact; therefore the patient had not had rhinorrhea at the time of the original cranial fracture. The fluid had now escaped through the dural suture lines into the extradural space and through this opening into the pharynx.

Subsequent Course.—There was no discharge of fluid after operation. Seven years later (April 19, 1941) the patient died of recurrence of the tumor; there was never recurrence of the rhinorrhea.

CASE 5.—*Postoperative defect in the ethmoid cells following removal of an orbital tumor by the transcranial route.*

R. H., a white woman aged 35, was seen on April 7, 1937. Immediately after removal of an intracranial and intraorbital dural meningioma, rhinorrhea appeared (fig. 5). It was clear that an ethmoid cell had been opened. On the following day the wound was reopened, and the open cell was found and covered with bone wax. A flap of orbital fascia was placed over the waxed opening and treated with 3.5 per cent solution of iodine to promote adhesions. Recovery was uneventful. There was no subsequent leak of cerebrospinal fluid.

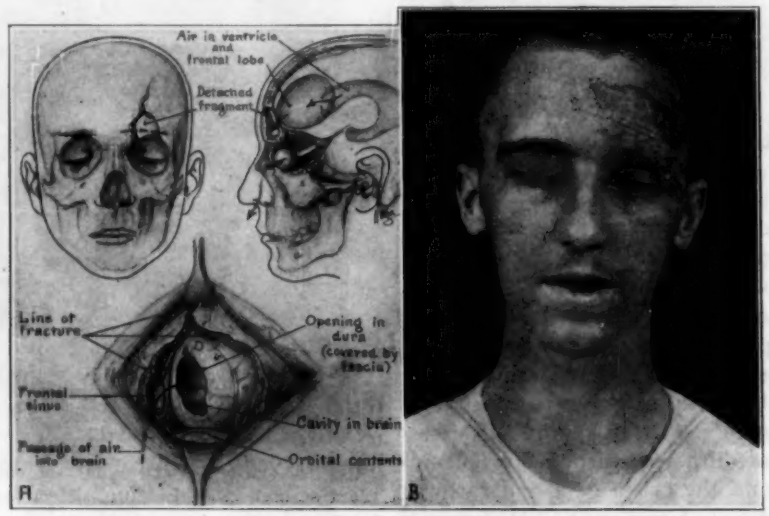

Fig. 2 (case 2).—*A*, drawings illustrating essentially the same condition as in case 1, i. e., advanced pneumocephalus with destruction of the frontal lobe and filling of the ventricular system. In this case the dural opening, which was covered with fascia, as in case 1, was also of a ball valve type, since the two openings were not superimposed. *B*, patient two weeks after operation. He was unconscious on admission to the hospital. At the present time, sixteen years after the operation, he is fighting with the United States Marines in the South Pacific.

CASE 6.—*Postoperative defect in the left petrous bone and the dura.*

E. W., a white woman aged 27, was seen on July 3, 1934. A cerebrospinal fistula from the left ear had persisted for four years after mastoidectomy. Meningitis was said to have been present at the time of the operation on the mastoid.

At operation a circular opening (about 0.5 cm. in diameter) was exposed in the roof of the petrous bone and about 2 cm. inside the skull (fig. 6). There was a defect in the overlying dura, and cerebrospinal fluid was escaping. Fascia from the temporal muscle was sutured over the dural defect. Then the bony defect was covered with wax.

Subsequent Course.—The patient recovered, with no subsequent drainage of spinal fluid.

CASE 7.—*Postoperative defect in the petrous bone and the dura.*

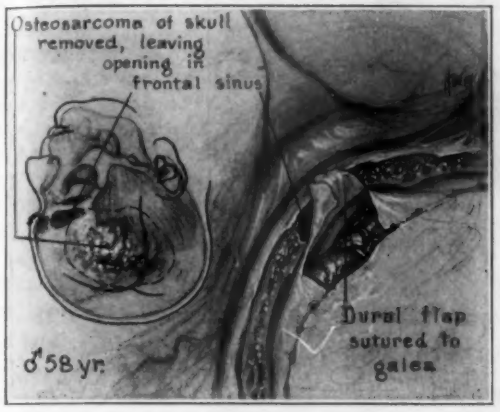

Fig. 3 (case 3).—Operative procedure for removal of an osteosarcoma of the skull: A large dural flap was turned down and the frontal sinus was opened and covered by a flap of dura, which was snugly sutured to the galea.

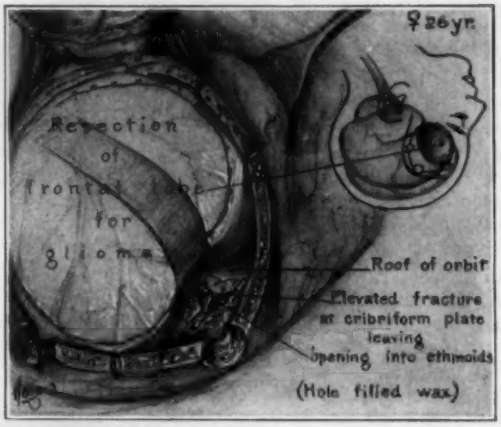

Fig. 4 (case 4).—An old elevated fracture of the cribriform plate, which had lain dormant for many years, was uncovered when the dura was stripped from it at operation for the removal of a tumor of the frontal lobe. The fluid leaked from the dural incision and passed through the old bony defect into the ethmoid cells; the opening was waxed.

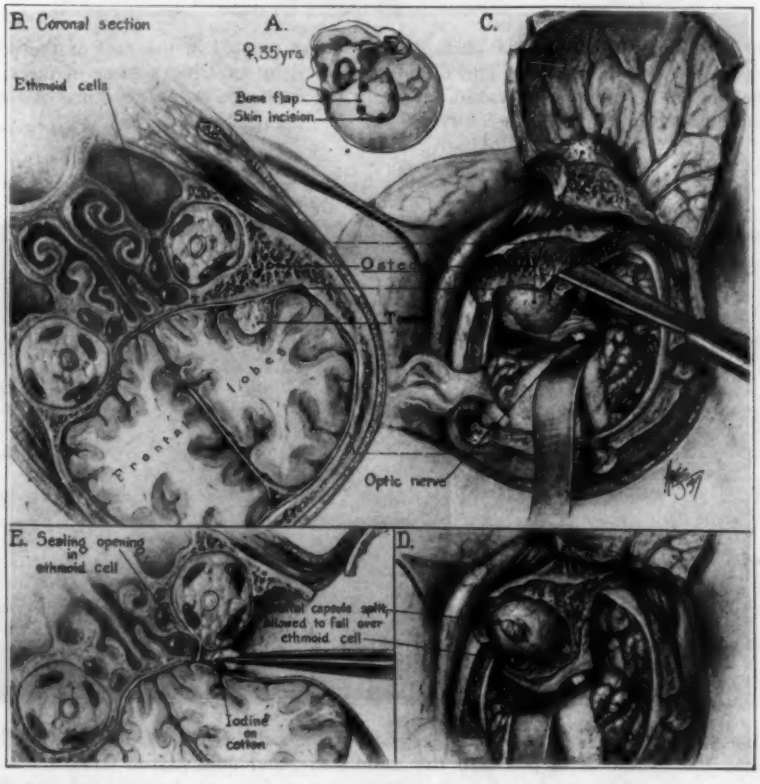

Fig. 5 (case 5).—When the hypertrophied bone caused by an overlying dural meningioma of the orbital roof was being chiseled away, an ethmoid cell was opened, and rhinorrhea followed. The wound was reopened, and a flap of the orbital capsule was thrown over the fistula and treated with 3.5 per cent solution of iodine to stimulate adhesions. In operations of this type the dural lining of the orbital roof is now stripped mesially, so that it can be used if a cell should be opened.

Fig. 6 (case 6).—Drawing showing the postoperative defect created in the roof of the petrous bone and the dura by a faulty operation on a mastoid. The dura was closed by suturing a piece of fascia from the temporal muscle, and the opening in the bone was waxed. During the exposure an old fracture of the petrous apex was disclosed, but it had nothing to do with the otorrhea.

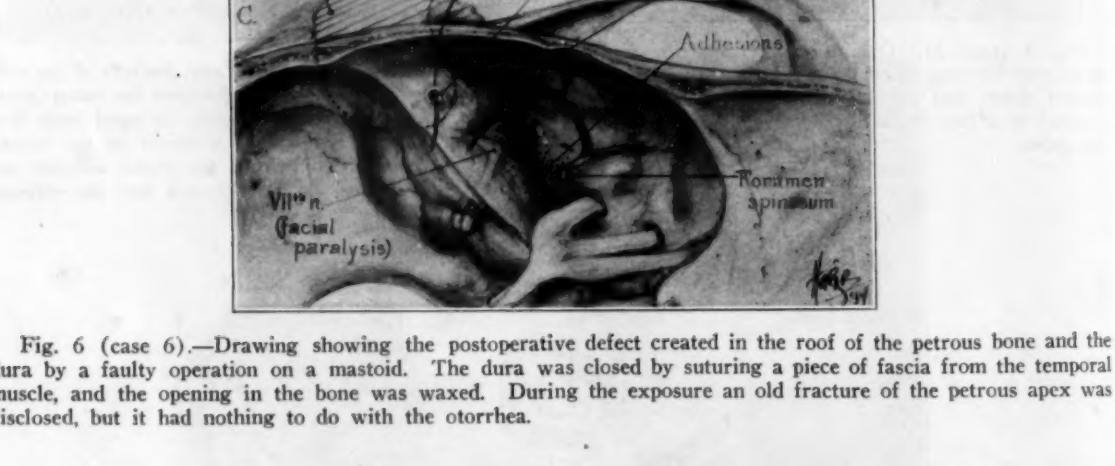

Fig. 7 (case 10).—*A*, operative sketch showing erosion of the petrous bone from an acoustic neuroma. After removal of this tumor the fistula developed into the middle ear, and fluid passed down the eustachian tube into the pharynx. *B*, postmortem photographs of both petrous bones, i. e. on the affected and the unaffected side. No defect was found in the petrous bone, but it was extremely porous. An attempt to close the fistula in the cartilaginous lining of the middle ear was unsuccessful. Some time later the patient died of meningitis—his third attack since the onset of rhinorrhea. How the fistula developed in the middle ear is not clear.

M. R., a white woman aged 26, was seen on Aug. 27, 1938. Otorrhea of five years' duration followed immediately after an operation on the mastoid. There was recovery from one attack of meningitis during this period.

At operation an opening (about 1 by 1 cm.) was located in the dura and in the roof of the petrous bone about 2 cm. from the lateral surface of the skull. The temporal lobe protruded through the dural opening and filled the bony defect. This fungus was cut away, the dural defect was closed with silk and a piece of fascia from the temporal muscle was sutured over the closed dura.

Subsequent Course.—The patient recovered, with no subsequent otorrhea.

CASE 8.—*Postoperative defect in the petrous bone and the dura.*

F. S., a white boy aged 10 years, was seen on Aug. 21, 1941. A periodic discharge of cerebrospinal fluid from the left ear was noticed after an operation on the mastoid four years before his admission to the hospital. The longest period in which the opening was closed was nine months; the patient never had meningitis.

An operation was performed on Aug. 21, 1941. Over the roof of the petrous bone, 1 cm. from the lateral surface of the skull, there was an opening as large as a lead pencil and a corresponding opening in the dura. Granulation tissue and a cerebral fungus filled the openings. The dural opening was closed with silk, treated with 3.5 per cent solution of iodine and covered with fascia from the temporal muscle. The opening in the bone was not waxed.

Subsequent Course.—No discharge of fluid was present at any time after operation.

CASE 9.—*Postoperative defect in the temporal bone and the dura posterior to the right mastoid.*

S. M., a white girl aged 11 years, was seen on Jan. 7, 1944. Since an operation on a mastoid six months previous to her admission to the hospital, there had been intermittent discharge of cerebrospinal fluid from the right ear—about a quarter of a pint (118 cc.) daily. A protruding fungus filled the external auditory meatus. She had survived with complete recovery one attack of meningitis and at the time of hospitalization had a maximum temperature of 100 F. daily; the pulse rate was from 120 to 140.

At operation an opening in the temporal bone back of the petrous portion and a defect in the dura about 1 cm. square were closed with sutures and not reenforced by fascia. The fungus was removed from the external ear.

Subsequent Course.—The wound in the external ear became infected. Cerebrospinal fluid did not leak at any time after the operation, but the fever and tachycardia persisted and gradually increased. On the nineteenth day her temperature rose to 105 F. and her pulse rate increased to 170; hemiplegia and coma followed, with death twenty-six days after operation. Multiple abscesses studded the right hemisphere; Staph. aureus was isolated. Sulfadiazine had been given by mouth since her entry into the hospital.

CASE 10.—*Rhinorrhea (otorrhea?) through a postoperative defect in the mastoid following removal of a tumor of the acoustic nerve; a fistula into the middle ear.*

L. T., a white man aged 48, was seen on March 4, 1937. After removal of a large tumor of the acoustic nerve (April 27, 1937) from which there was extensive destruction of the petrous bone, rhinorrhea appeared and persisted (fig. 7*A* and *B*). I was puzzled that rhinorrhea and not otorrhea developed and assumed that the fluid had in some way entered the eustachian tube mesial to the ear drum and then entered the pharynx.

After two attacks of meningitis—(1) pneumococcus type XXIX (Dec. 20, 1937) and (2) Staph. aureus (March 2, 1938)—both of which cleared promptly and miraculously with sulfanilamide, which was just then beginning to be used, the cerebellar wound was opened and the hollow in the petrous bone painstakingly waxed (March 4, 1938), but without any effect on the drainage of cerebrospinal fluid.

Dr. Baylor then found the drum bulging with fluid and injected methylthionine chloride (methylene blue) into it. A blue-stained fistula was located in the posterior wall of the middle ear. This cartilaginous opening was sutured and the adjacent mastoid waxed. The wound broke down with infection, and the sutures were extruded.

The rhinorrhea persisted. Several weeks later, on April 6, 1938, he had another attack of meningitis (Staph. aureus) and died.

CASE 11.—*Spontaneous rhinorrhea.*

G. S., a white man aged 39, was seen on Sept. 15, 1943. The patient was referred by Dr. E. H. MacKinlay, of McConnellsburgh, Pa.

His complaint was "water flowing from the nose." He had had severe bilateral sinusitis ten years before I saw him; he reported drainage of pus for one year and headaches during the entire time. He has had no trouble with sinuses since then. He had had two unconscious spells: The first, a year before admission to the hospital, lasted two to three hours; the second, one week before, lasted thirty-six hours. The present illness began four months preceding hospitalization, when clear, colorless fluid began to drain from the right side of the nose. There had been no antecedent injury or infection. This drainage had been almost constant for four months. When he was standing or sitting the fluid went down the back of his throat. When he bent forward it poured out of the right nostril in a steady stream. Physical and neurologic examinations gave normal results except for the draining fluid. When he was bending forward about 2 cc. of clear colorless fluid was collected in two minutes. This came exclusively from the right nostril; however, if he turned to the left, the fluid came from the left nostril. For several years he has had occasional generalized convulsions. The blood pressure was 130 systolic and 80 diastolic; a Wassermann test of the blood gave negative results. Roentgenograms of the skull were normal, and a reexamination after the lesion was disclosed at operation did not reveal the small openings in the bone.

A diagnosis of spontaneous rhinorrhea through a frontal sinus of undetermined origin, probably from the right sinus, was made. An exploratory operation on the small right frontal lobe was performed on Sept. 20, 1943. A slender strand of tissue slightly larger than the lead in a pencil and 1 cm. long was passed from the tip of the frontal lobe (fig. 8) through an opening in the dura and skull—presumably the outer part of the frontal sinus—but when a probe was passed into the opening a little orbital fat protruded and was excised. It is doubtful, therefore, that this opening passed into the frontal sinus. The strand of tissue bridging the subdural space was excised for microscopic study; the

tissue was of nondescript fibrous character, condensed into two circular strands; no definite nerve tissue could be identified. The dura was stripped from the anterior fossa, the bony opening plugged with wax and a piece of temporal fascia placed over the opening of the dura on its outer surface. A 3.5 per cent solution of iodine was applied to stimulate adhesions.

Subsequent Course.—The rhinorrhea continued after operation, but the patient stated that the quantity was about half as much as before. Two months later there had been no change. The frontal region was reexplored Nov. 30, 1943, but the opening was sealed over perfectly. It was then supposed that another fistula was probably on the left side. The left frontal lobe was explored on Dec. 11, 1943, and a similar strand of tissue was found at exactly the same spot as on the right. It was shorter and broader than that in the right—perhaps 0.5 cm. long and as large as a slate pencil. The arachnoid could be seen passing from the frontal lobe around the strand of tissue and was filled with cerebrospinal fluid. There were a defect in the dura and a bony opening—possibly into the outer part of the frontal sinus. The bridge of tissue was cut through, but it was too short to excise for microscopic study. The cisterna at the chiasm was opened to provide room for the operative attack on the fistula. The dura was not stripped from the floor of the skull, but a piece of

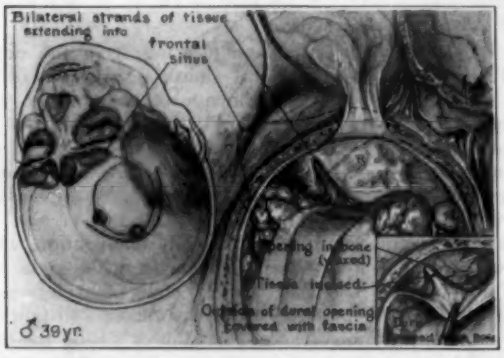

Fig. 8 (case 11).—In this case of spontaneous rhinorrhea a strand of tissue was found running through the dura and the bone and an arachnoidal sheath filled with fluid surrounded this strand of tissue. The same condition was disclosed on the opposite side, but closure of both fistulas did not stop the rhinorrhea. They probably, therefore, did not enter the frontal sinuses, as was hoped at the time of the operation. The fistula causing the rhinorrhea was therefore not found. This is the only case in which the fistula was not located.

temporal fascia was sutured over the opening and treated with 3.5 per cent solution of iodine to stimulate adhesions. The iodine solution was also applied to the opening in the arachnoid. It should be noted that there was evidence of congenital malformation of the left frontal lobe in that the vascular pattern was abnormal—there being two large and tortuous veins running across the outer surface of the lobe from the sylvian fissure to the longitudinal sinus. The unconscious spells were doubtless due to the congenital malformation (on the patient's first admission to the hospital ventriculography showed a normal ventricular system).

After operation the flow of cerebrospinal fluid was unchanged, and at the time of this writing (nine months later) it persists to the same degree. The findings at operation therefore did not account for the rhinorrhea. The openings in the bone could not have been into the frontal sinus.

SUMMARY AND CONCLUSIONS

Though not a common condition—11 cases in nearly twenty years—continuing rhinorrhea and otorrhea nearly always demand surgical closure of the opening in the dura or the bone, preferably both. Although spontaneous closure of the fistula does occur, it is not common, and it is not safe to delay operation in the hope that such closure may take place. The operation itself is practically free of danger. Death following closure of a fistula is due to preexisting intracranial infection—usually one or more abscesses in the brain. The fistula may be closed in several ways: (1) suturing the dural opening; (2) suturing when possible a transplant of fascia over the dural defect; (3) suturing snugly to the overlying tissues a flap of dura or any soft tissue which has been turned over the bony opening; (4) covering the bony opening with bone wax.

Eight of the 11 patients whose cases are included in this report were permanently cured. Two (cases 9 and 10) died subsequently of intracranial infection; in 1 the infection was present at the time of operation, and in the other it appeared subsequently. One patient (case 11) remained unimproved nine months after operation; congenital openings in the dura and bone were found and closed on each side. At the time they were thought to enter the frontal sinuses, but this assumption was incorrect, because there was no benefit. The real fistula therefore was not located.

Usually the location of the fistula is readily determined by the site of a fracture or by an operation at which the opening in the bone and the dura was created. But disclosure of the fistulous tract may be exceedingly difficult, perhaps even impossible, as in case 11. In this case there has been no definite indication even of the side of the fistula. In case 10 the fistula into the middle ear was found only after injecting methylthionine chloride (methylene blue) through the bulging drum. In this case closure of the fistula in the cartilaginous wall was unsuccessful.

Pneumocephalus with a large unilateral defect in the frontal lobe and complete filling of the ventricular system was present in 2 cases (1 and 2) and was promptly cured after the fistula was closed.

For fistulas through the frontal sinus there are two methods of approach: (1) by elevating the depressed fracture, suturing or covering the

defect with fascia and replacing the depressed fracture; (2) if there is no depressed fracture, by exposing the frontal region through a unilateral frontal bone flap with a concealed incision. This is preferable to cutting away the walls of the frontal sinus and leaving an unsightly deformity. If the side of the fistula cannot be determined, the same unilateral exposure is made on the suspected side (suggested by the side of the nose into which the cerebrospinal fluid drains), and if the opening is not found the same procedure is indicated on the other side later. Two such procedures are preferable to the single large bilateral exposure, which uncovers and usually requires ligation of the longitudinal sinus.

Drainage of cerebrospinal fluid from the nose is not pathognomonic of a fistula into the frontal or the ethmoid sinus but may occur through the mastoid bone into the middle ear and the eustachian tube, as in case 10; this, however, is exceptional.

PLASMA CELL MASTITIS

REPORT OF FIVE ADDITIONAL CASES

WILLARD H. PARSONS, M.D.; JOHN C. HENTHORNE, M.D., AND R. LEE CLARK JR., M.D.

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Although plasma cell mastitis is a relatively uncommon disease, it is important because of its clinical resemblance to carcinoma of the breast. The resemblance is so close, as a matter of fact, that in at least half of the recorded cases primary radical mastectomy was performed, on the assumption that the inflammatory swelling was malignant.

This clinical entity (we are among those who accept it as such) was first described under the name plasma cell mastitis by Adair [1] in 1933. Prior to his contribution, as Payne and his associates [2] have pointed out, the condition was described in the German literature under the term mastitis obliterans, and it is possible that it has also been discussed under still other designations. The indolent form of mastitis, described by Bell [3] as pseudotuberculosis, seems to be this same disease. Adair's contribution, however, is so outstanding that the term plasma cell mastitis will probably continue to be favored, especially in the United States.

A description of plasma cell mastitis is included in several recent medical textbooks,[4] and to date some 45 cases have been formally reported in medical literature [5] or have been mentioned in discussions.[6]

Plasma cell mastitis, according to the various descriptions in the literature, is characterized by a unilateral painless tumor which occurs in parous women. Sometimes mild and evanescent signs of inflammation are present in the course of its development, and occasionally there is a watery or a creamy discharge from the nipple. Its most distinctive clinical feature, as already pointed out, is its striking resemblance to mammary carcinoma. It is not usually tender. It is often so adherent to the skin as to produce orange peel dimpling. The nipple is frequently retracted. Finally, the axillary lymph nodes are likely to be enlarged.

The gross lesion of plasma cell mastitis appears as a yellowish brown discoloration of the mammary tissue, often associated with formation of an abscess. The contents of the abscess and of the contiguous ducts are puriform or butter-like. The histologic features of the lesion are: formation of an ulceration of the normal epithelium of the ducts, which is replaced by granulation tissue, whence the term mastitis obliterans; formation of foreign body giant cells, whence the term pseudotuberculosis, and periductal collections of plasma cells and other leukocytes, whence the term plasma cell mastitis. Some authors have reported hyperplasia of the ductile epithelium and intraductal collections of colostrum cells. Others have noted large numbers of eosinophils in the inflammatory exudate, and still others have observed sheaves of fatty acid crystals and other evidences of the presence of lipoid substances, such as foamy histiocytes and droplets of fat within the plasma cells.

The 5 specimens from cases of plasma cell mastitis reported on in this communication were collected from a total of 1,500 specimens from

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Read before the Section on Surgery, General and Abdominal, at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Adair, F. E.: Plasma Cell Mastitis—A Lesion Simulating Mammary Carcinoma: A Clinical and Pathologic Study with a Report of Ten Cases, Arch. Surg. **26**:735-749 (May) 1933.

2. Payne, R. L.; Strauss, A. F., and Glasser, R. D.: Mastitis Obliterans, Surgery **14**:719-727 (Nov.) 1943.

3. Bell, E. T.: A Text-Book of Pathology, ed. 3, Philadelphia, Lea & Febiger, 1938, pp. 408-415.

4. (*a*) Cheatle, G. L., and Cutler, M.: Tumors of the Breast: Their Pathology, Symptoms, Diagnosis and Treatment, Philadelphia, J. B. Lippincott Company, 1931, pp. 298-304. (*b*) Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 547-548. (*c*) Geschickter, C. F.: Diseases of the Breast: Diagnosis, Pathology, Treatment, Philadelphia, J. B. Lippincott Company, 1943, pp. 161-162.

5. (*a*) Cutler, M.: Benign Lesions of the Female Breast Simulating Cancer, J. A. M. A. **101**:1217-1222 (Oct. 14) 1933. (*b*) Rodman, J. S., and Ingleby, H.: Plasma Cell Mastitis, Ann. Surg. **109**:921-930 (June) 1939. (*c*) Miller, J. K.: Plasma Cell Mastitis: A Pathologic Entity, Am. J. Surg. **43**:788-793 (March) 1939. (*d*) Cromar, C. D. L., and Dockerty, M. B.: Plasma Cell Mastitis, Proc. Staff Meet., Mayo Clin. **16**:775-783 (Dec. 3) 1941. (*e*) Adair.[1] (*f*) Ewing.[4b]

6. (*a*) Moore, J. J., in discussion on Cutler.[5a] (*b*) Frank, L. W., in discussion on Rodman and Ingleby.[5b]

female breasts studied during the past six and a half years from the services of the Vicksburg Hospital and from other sources in Mississippi. Clinical data are complete for only 2 of the cases, but reports on the other 3 are included to give some index of the general incidence of this condition. As several authors have pointed out, any review of a reasonably large number of cases of disease of the female breast is likely to reveal a few cases of plasma cell mastitis.

REPORT OF CASES

CASE 1.—Mrs. L. E. A., a white woman aged 43, was admitted to the Vicksburg Hospital in the surgical service of one of us (W. H. P.) on Jan. 26, 1940. On January 3, while bathing, she had noticed a "lump" in the right breast. There had been no pain or discomfort at any time, but in the next two weeks the mass had become larger and the skin over it had become slightly reddened.

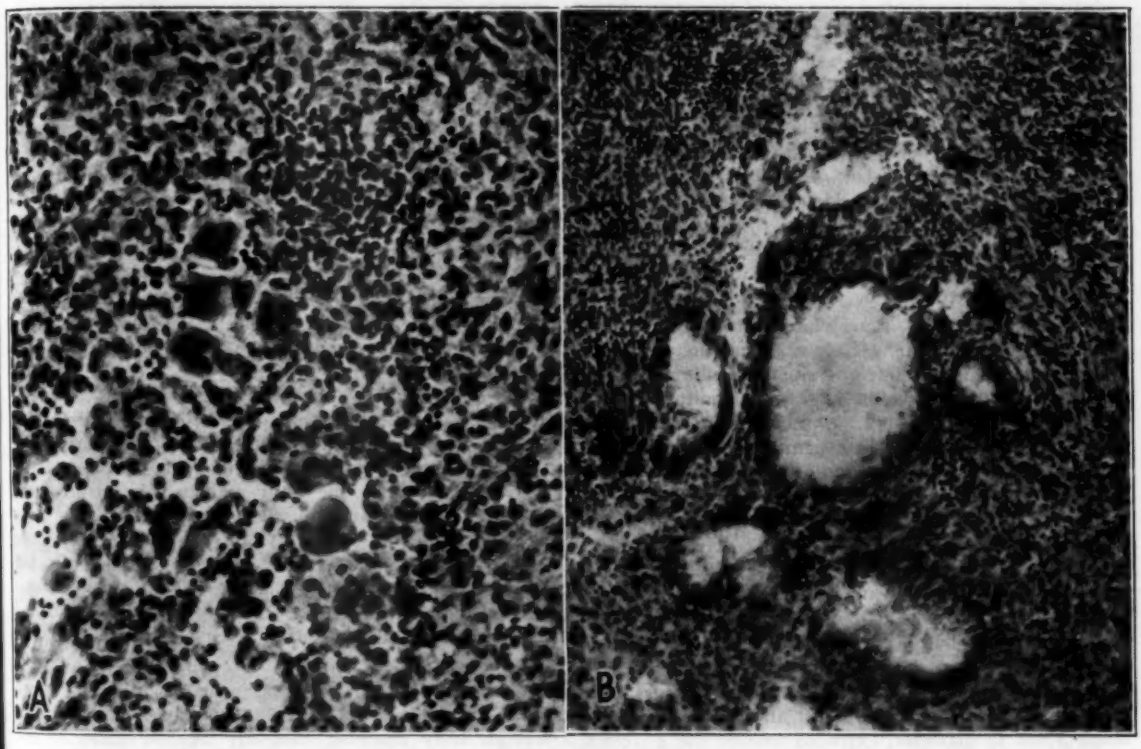
The patient's family history was not significant. Her cervix uteri had been cauterized at the Vicksburg Hospital in July 1939, and her appendix had been removed elsewhere sixteen years before. She had been married twice. The second marriage was without offspring, but she had had three children by her first husband, and during this marriage she had had a therapeutic abortion, the details of which were unknown.

Objectively both breasts seemed equal in size, but in the right breast, just below the nipple in the 6 o'clock position, there was a definite orange peel dimpling of the skin, which was slightly reddened. Palpation over this area revealed an underlying tumor, which was 2.5 cm. in diameter and was attached to the skin; it was not tender. The axillary lymph nodes could not be palpated. The physical examination otherwise gave essentially negative results.

Urinalysis revealed no abnormality. The hemoglobin content was 15.3 Gm. (Sahli). The erythrocytes numbered 4,640,000 and the leukocytes 16,700 per cubic millimeter. The neutrophilic percentage was 68. Flocculation tests for syphilis gave negative results, and roentgenologic examination of the chest for possible metastases revealed no abnormality.

Radical mastectomy, on the right side was performed Jan. 27, 1940, with the patient under cyclopropane-ether anesthesia, on the assumption that the lesion in the breast was malignant. The pathologic report was as follows (J. C. H.):

The specimen consisted of a mammary gland removed by radical mastectomy together with the pectoral muscles and the axillary lymph nodes. Beneath the nipple in the 6 o'clock position was an abscess 3 cm. in diameter filled with yellowish brown, semiliquid, putty-like material. The shaggy brownish discoloration of the wall of the abscess extended into the contiguous mammary tissue and skin. The ducts of the remainder of the breast were distended with inspissated brown fluid, which was easily expressed. The axillary nodes were soft and gray and were enlarged to a diameter of 1.5 cm.



Plasma cell mastitis. *A*, inflammatory exudate containing foreign body giant cells and plasma cells (hematoxylin and eosin; × 200). *B*, clear areas, which are evidently produced by sheaves of fatty acid crystals, surrounded by giant cells (hematoxylin and eosin; × 115).

Histologic examination revealed the wall of the abscess to be lined with granulation tissue infiltrated with a variety of leukocytes, including plasma cells, neutrophils and giant cells of the foreign body type (*A* of the figure). In several areas there were collections of clear paraffin-like material, which on closer inspection presented needle-shaped crystals arranged radially around the periphery. These clear areas were surrounded by giant cells (*B* of the figure). Elsewhere in the tissues surrounding the abscess periductal fibrosis and infiltration of leukocytes were observed. Colostrum cells were found in a few of the ducts, but hyperplasia of the epithelium was not notable. The axillary lymph nodes showed fatty changes and dilatation of the sinusoids.

The original diagnosis was pseudotuberculosis with formation of an abscess and diffuse comedomastitis. Later, when the contributions to the literature on plasma cell mastitis came to our attention, this term was substituted for pseudotuberculosis, and the same change in terminology was made in cases 3, 4 and 5, which had already been observed.

The postoperative course was uneventful, and the patient was discharged on the thirteenth day after operation. The wound healed by primary intention.

The patient has been observed on several occasions since her discharge. On Dec. 4, 1940 she was delivered of a normal child, and on March 14, 1941 a calculus was removed from the left kidney. She was last seen April 8, 1944, for symptoms referable to the menopause. No changes were observed in the remaining breast during pregnancy or menopause.

Case 2.—Mrs. W. J. B., a white woman aged 42, was first seen by one of us (R. L. C.) on Aug. 15, 1940. She had had pain in the right nipple for the past three years, and a month before she was admitted to our service she had discovered a tumor in this location. The tumor had been slightly painful from the time of its discovery, and at the time of consultation soreness extended into the right axilla.

The patient was married and had two children, the youngest of whom was 10 years old. The left ovary and the appendix had been removed in 1922 and the uterus, tubes and right ovary in 1932. For the past four or five years she had had recurrent attacks of pyelitis, the last of which had occurred about two months before consultation.

Objectively the breasts, which were pendulous, were equal in size. In the right breast an area of erythema, about 3 cm. in diameter, extended toward the 2 o'clock position from the edge of the nipple, which was retracted. Underlying this area there was a dense, slightly irregular, moderately tender tumor of approximately the same size. The axillary lymph nodes were not palpable.

Urinalysis revealed no abnormalities, and flocculation tests for syphilis gave negative results. The hemoglobin content was 16 Gm. (Sahli). The erythrocytes numbered 4,880,000 and the leukocytes 9,950 per cubic millimeter. The neutrophilic percentage was 67.

The involved portion of the right breast was removed on Aug. 20, 1940 with the patient under anesthesia induced with intravenously administered pentothal sodium, and was described as follows (J. C. H.):

The specimen consisted of a lobule of fibrous mammary tissue measuring 2.5 by 2 by 2 cm. The cut surface contained an area of shaggy brown discoloration, and putty-like material could be expressed from the ducts.

Histologic examination revealed periductal accumulation of leukocytes, including many plasma cells and a moderate number of foreign body giant cells. The exudative process had obliterated the architecture of the lobule. Colostrum cells were observed in several of the dilated ducts.

The diagnosis was plasma cell mastitis.

The patient was dismissed from the hospital the day after operation. Observation on Sept. 13, 1940 showed the wound well healed and the breast apparently normal. The local findings were the same on Oct. 3, 1940. The patient at this time was suffering from acute tonsillitis. Treatment was carried out elsewhere, and tonsillectomy at a later date was advised, but the advice had not been accepted up to the time of this report.

The patient was again seen Dec. 10, 1940, for a digestive disturbance. The breast revealed no abnormalities. On March 20, 1941, five months after removal of the mammary tumor, she presented herself, complaining of swelling of the right breast, discharge from the nipple and pain extending down the right arm to the elbow. Examination showed the breast to be tender and inflamed in the region of the scar, and palpation revealed a small swelling just beneath the incision. When the affected area was incised, a small amount of thick yellow pus was evacuated. All evidences of inflammation had subsided within two weeks.

When the patient was last seen, on June 11, 1942, she had had no further difficulties referable to the breast.

Case 3.—The biopsy specimen in this case was obtained on March 10, 1938. Histologic examination revealed a periductal inflammatory reaction, including fibrosis, leukocytic infiltrations and collections of blood pigment. It was thought that the lesion represented an inflammatory change, such as might result from trauma.

On April 12, 1938, in submitting for study the entire mammary gland and a portion of the pectoralis major muscle, the surgeon wrote that the patient had continued to have symptoms and that the lesion had become adherent to the skin and had penetrated the fascia of the pectoral muscle. He was naturally concerned over the possibility of cancer. Nothing to suggest this diagnosis, however, was found in the specimen, which revealed plasma cells, foam cells and foreign body giant cells. The original diagnosis of pseudotuberculosis was later changed to plasma cell mastitis.

Case 4.—The biopsy specimen in this case was obtained on Sept. 21, 1939. Examination revealed a foreign body reaction, evidently against material extravasated from the ducts. A diagnosis of pseudotuberculosis (later plasma cell mastitis) was made.

Case 5.—The biopsy specimen in this case was obtained on Oct. 30, 1940. The diagnosis was pseudotuberculosis (later plasma cell mastitis) associated with comedomastitis.

COMMENT

The clinical features of the cases of plasma cell mastitis reported here duplicate those common to most of the other recorded cases. In case 1, for instance, the resemblance to carcinoma of the breast was embarrassingly close, and the associated leukocytosis observed in this case has also been recorded by Geschickter.[4c] In case 2 the lesion was more definitely suggestive of an inflammatory process, although it was only moderately tender, and the nipple was retracted.

The discharge from the nipple in this case was similar to the discharge in other recorded cases, though in this instance it was part of the recurrent and not of the primary lesion.

Some features of this disease have not previously been reported, including recurrence of the lesion, which was observed in cases 2 and 3, and diffuse comedomastitis, which coexisted in the excised portions of the mammary glands in cases 1 and 5. It is possible that material high in lipid content may be contributed to the inflammatory area as the result of the presence of comedomastitis.

In case 2, the patient had badly diseased tonsils, and the speculation is advanced that the focal infection may have contributed to the development of the mastitis, because in another case of indolent mastitis observed by one of us (R. L. C.) the patient continued to have trouble with the breast until tonsillectomy was carried out, after which, without other therapy, the mastitis promptly subsided.

It is interesting that in case 1 the patient went through a normal pregnancy in the same year that her breast was removed without the development of mastitis in the remaining breast. It is also interesting that in case 2 the patient had been castrated five years before the onset of symptoms referable to the breast and the course of the plasma cell mastitis covered three years, which is an unusually prolonged time for this condition. The apparent difference in the endocrine constitution in the 2 cases seems worthy of comment.

SUMMARY AND CONCLUSIONS

A study of 5 cases of plasma cell mastitis, which are reported herewith, leads us to agree with other observers that this disease, which is a periductal inflammatory reaction caused by the extravasation of material from the ducts into the periductal fibrous tissue, is a true clinical entity. The morphologic characteristics of the lesion apparently depend on the lipid character of the ductal contents.

The speculation is advanced that if comedomastitis, which was associated with the plasma cell mastitis in 2 of the reported cases, exists prior to the extravasation of material from the ducts it may be responsible for the large quantity of material high in lipid content in the inflammatory area. Focal infection is also suggested as one of several possible causes of ulceration of the ducts and of extravasation of their contents.

ABSTRACT OF DISCUSSION

Dr. Warren H. Cole, Chicago: Dr. Parsons has called attention to the marked similarity of plasma cell mastitis to carcinoma. I should like to emphasize the difficulty in distinguishing plasma cell mastitis from fat necrosis in certain cases. Obviously, fat necrosis exhibiting large areas of liquefied fat bears little resemblance to plasma cell mastitis as described eleven years ago. However, in fat necrosis with minimal liquefaction of fat the histologic features may be identical. Although not appreciably emphasized previously, a study of sections from fat necrosis which are well advanced toward resolution will show heavy infiltration of plasma cells, indicating that the plasma cell itself is not specific for the lesion under discussion. Likewise, lymphocytic infiltration, giant cells and moderate epithelial hyperplasia will also be encountered in fat necrosis. It is true that the histologic resemblance to carcinoma is different in the two lesions, in so far as plasma cell mastitis resembles comedo carcinoma, whereas the hyperplasia in fat necrosis resembles a medullary type of carcinoma. It is proving extremely difficult to classify a case recently observed at the Illinois Research Hospital. This patient was 41 years of age. She had four children, the youngest of whom was 17 months old. The mass in the breast was only of six weeks' duration and for the first two or three weeks showed the typical mild inflammatory reaction encountered in plasma cell mastitis. Sections showed a moderate number of plasma cells along with the other features of mild inflammation, including numerous giant cells. All of three cultures of liquefied sebaceous-like material and other parts of the lesion gave negative results. In most cases of plasma cell mastitis, as reported in the literature, there is mild evidence of fat necrosis, as suggested by fat globules in the giant cells and plasma cells. It appears that in both lesions fat necrosis may be the most important factor, thereby explaining the inflammatory reaction observed histologically. In fat necrosis trauma can be considered as the initial trigger mechanism, which, however, is lacking in plasma cell mastitis. Although, occasionally, cultures are reported as giving positive results in plasma cell mastitis, there is no conclusive evidence that a pathogenic bacterium is the cause. Nevertheless, the inflammation is obviously secondary to some mechanism. If it is infection the cause must be either an extremely mild pathogenic bacterium or possibly a virus. The multiplicity of virus infections, including such diseases as venereal lymphogranuloma, which exhibits inflammation frequently progressing to suppuration, is sufficient evidence to support this possibility. The fact that fat necrosis may be the chief factor responsible for the inflammatory reaction in both diseases is not new, since Ewing in Adair's original article (1933) stated: "It may therefore be concluded that while bacterial infection is probably a necessary factor in the process, its influence is less prominent than the chemical effect of decomposing fatty material."

I thought that my idea on the prominent role which the chemical effect of decomposing fat material assumes in plasma cell mastitis was new, but my recent discovery of this statement by Ewing indicates that he had that point in mind at the time of the original description.

Dr. R. L. Sanders, Memphis, Tenn.: The condition described is rare. Its chief interest lies in its resemblance to carcinoma. The fact that the essayists have observed plasma cell mastitis in 5 of 1,500 pathologic specimens indicates that, despite its rare incidence, it should be kept in mind in the differential diagnosis. Clinically, plasma cell mastitis may be divided into two phases: acute and residual. The acute phase, which presents the signs and symptoms of a diffuse inflammatory lesion radiating from the nipple, is frequently sudden in onset, though usually it is not severe and

does not proceed to formation of an abscess. Instead, after several days the acute symptoms subside, and occasionally the condition will clear up completely. In many cases after subsidence of the acute manifestations there remains a firm, often irregular tumor which may present all the signs of carcinoma. After this stage is reached, improvement takes place so slowly as to be imperceptible. If the patient is seen during the acute stage, the distinction between an inflammatory and a malignant lesion should present little difficulty. After this time one must rely chiefly on the history of an acute inflammation which has subsided. Carcinoma is progressive and, even though accompanied by inflammation, continues to spread and become increasingly severe. A discharge from the nipple is also indicative of plasma cell mastitis, and of additional diagnostic value is the fact that the condition generally develops in the nonlactating breast. The diagnosis is not always easy, as the history may be indefinite and the clinical picture may vary from the usual pattern. This is illustrated in the first case presented by the essayists, in which the patient had no pain, discomfort or discharge from the nipple. Adair stated that in 6 of the 10 cases which he reported the tumor was regarded as malignant by several men with extensive experience in diagnosis of cancer. Of 24 cases reported by Cromar and Dockerty at the Mayo Clinic, a diagnosis of cancer was made in 17. In some cases the diagnosis may be established by biopsy, yet here again there is much room for error because of the varied histologic picture. In only 2 of the 24 cases at the Mayo Clinic was the pathologist's diagnosis plasma cell mastitis. During the acute stage, only conservative treatment is indicated. Once the symptoms have subsided, however, local excision of the tumor is advisable. The prognosis in these cases is unknown; since the lesion may be almost indistinguishable from carcinoma histologically as well as clinically, one may assume that it is of the precancerous type. Every attempt should be made to establish the diagnosis in order to avoid a radical operation; if this cannot be done with certainty, then one should not hesitate to perform a total mastectomy. It is better to follow this course and perhaps accept credit for the cure of a supposed carcinoma than to withhold the total operation on the slight chance that the condition might not be malignant.

Dr. Frank E. Adair, New York: The subject has been thoroughly discussed, but microscopic slides are necessary to show why pathologists have been confused by the pathologic picture. I am delighted that Dr. Parsons has contributed his 5 cases to the literature, because I have become discouraged wondering whether or not the subject was going to die slowly. A slide will show why pathologists have difficulty in making a diagnosis. The plasma cell denotes chronicity, and in cases of plasma cell mastitis the whole field is infiltrated with many of these plasma cells, in which the nucleus is excentrally placed. The histologic changes in the ducts have added to the great confusion of the pathologists—the people who seemed to have the greatest interest and who sent to me for slides after I reported my cases eleven years before the present report. There is a great heaping up of the lining cells of the ducts, and many pathologists who wrote to me for the slides told me that they had always called this condition comedo carcinoma because the cells lining the ducts were piled up eight and ten rows high. That is the reason, I think, why there has been a good deal of question in the minds of some of the pathologists about plasma cell mastitis.

Dr. John C. Henthorne, Vicksburg, Miss.: Dr. Cole's comments about the relation of fat necrosis to plasma cell mastitis are pertinent, because after all both conditions seem to be the result of extravasation of lipid material into the fibrous tissue. One lesion is produced by extravasation of fat from the interstitial tissue, and the other, plasma cell mastitis, may possibly be produced by extravasation of lipid material from the contents of the ducts. Whether or not plasma cell mastitis is produced by an infectious agent has not been investigated, possibly because the material after it has been excised from the breast is not suitable for inoculation of animals by the time the diagnosis is established. Inoculation of animals with suitable material should be done, but it is my opinion that most of the authors who have contributed to the subject have the impression that an infectious agent is not responsible for the disease. Dr. Sanders' discussion of the clinical features of plasma cell mastitis is especially interesting, since he was able to think back over his experience and recall certain cases of mammary tumor that might fall into this category.

ROENTGEN FEATURES OF CHRONIC TUBERCULOUS PERITONITIS

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Most authorities agree that the clinical diagnosis of tuberculous peritonitis is difficult.[1] The roentgenologic features of this disease were reported by Ritvo [2] and Soper [3] in their studies of the small intestine. Schatzki [4] likewise found an abnormal small intestinal pattern accompanying this disease. Since his investigation particular attention has been paid at the Massachusetts General Hospital to the possibility of establishing by roentgen examination a preoperative diagnosis; the condition of 3 patients who were admitted to the hospital subsequently was correctly diagnosed by the examining radiologist. The present paper presents these 3 cases and 3 additional proved cases of tuberculous peritonitis in which complete roentgenologic study of the large and the small bowel revealed certain characteristics.

Infection of the peritoneal surfaces with the tubercle bacillus may be divided into two main types, *acute* and *chronic*. The acute type may be further divided into two forms: (*a*) acute miliary tuberculosis of the peritoneum as part of a widespread hematogenous dissemination, the changes in the peritoneum being overshadowed by the primary process, and (*b*) acute localized peritonitis with involvement of a few mesenteric glands and the adjacent peritoneum. In a small percentage of cases of the localized type of peritonitis, owing to lowered resistance of the host or to high virulence of the organism, the tubercles break down and invade the greater part of the peritoneum, giving rise to *chronic* tuberculous peritonitis.

Acute localized peritonitis, which is not always recognized clinically, is usually found in children. No roentgenologic studies of this form were reported in the literature which I reviewed. In the majority of instances the process remains localized and results in caseation, fibrosis and calcification. Gibson [5] studied a group of 200 children and found 19 to have calcification of the abdominal lymph nodes, in 5 of whom there was indisputable proof of tuberculosis elsewhere. Thorough examination of the remaining 14 did not reveal the primary focus. He concluded that this disease should be suspected in children who give a positive reaction to the tuberculin test, whose normal growth has been interrupted and who have vague abdominal symptoms. Frank [6] expressed the opinion that tuberculous peritonitis is more common than is generally recognized. He found local peritoneal involvement in the majority of the 29 cases of tuberculous enteritis which he studied at autopsy. It is the experience of most radiologists who view a large number of roentgenograms of the abdomen that the finding of calcified lymph nodes is fairly frequent.

PATHOLOGY

Chronic tuberculous peritonitis is considered by pathologists to be a secondary infection in all cases.[7] Crawford and Sawyer,[8] in a study of 1,400 autopsy records, found 966 cases in which some form of tuberculosis was present. Of the 966 there were 645 cases of intestinal tuberculosis, in 73 of which peritonitis was a complication. In the majority of the 73 cases peritonitis was

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1. (*a*) Blake, J. A.: Tuberculous Peritonitis, in Nelson's Loose Leaf Surgery, New York, Thos. Nelson & Sons, 1941, vol. 5, chap. 1, pp. 35-41. (*b*) Pincoffs, M. C., and Boggs, T. R., in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1921, vol. 3, pt. 2, pp. 250-268. (*c*) Stein, I. F.: Oxygen Pneumoperitoneum in the Diagnosis and Treatment of Tuberculosis of the Genitalia, Intestines and Peritoneum, Surg., Gynec. & Obst. **58**: 567-577, 1934.

2. Ritvo, M.: Roentgen Diagnosis of Lesions of the Jejunum and Ileum, Am. J. Roentgenol. **23**:160-169, 1930.

3. Soper, H. W.: Roentgen-Ray Diagnosis of Lesions of the Small Intestine, Am. J. Roentgenol. **22**: 107-119, 1929.

4. Schatzki, R.: Small Intestinal Enema, Am. J. Roentgenol. **50**:743-751, 1943.

5. Gibson, C. B.: Calcified Abdominal Lymph Nodes, Am. Rev. Tuberc. **29**:447-460, 1934.

6. Frank, L. W.: Tuberculous Peritonitis, Am. Rev. Tuberc. **36**:279-282, 1937.

7. (*a*) Boyd, W.: Tuberculous Peritonitis, in Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1936, pp. 623-624. (*b*) MacCallum, W. G.: Tuberculous Peritonitis, in A Textbook of Pathology, ed. 6, ibid., 1936, pp. 652-654.

8. Crawford, P. M., and Sawyer, H. P.: Intestinal Tuberculosis in 1,400 Autopsies, Am. Rev. Tuberc. **30**:568-583, 1934.

thought to have followed perforation of ulcers and in a lesser number, to have been due to spread along the lymphatics to the mesenteric lymph nodes, with subsequent generalized peritonitis; in a few, not associated with intestinal ulceration, it was ascribed to general hematogenous miliary tuberculosis. Two forms of pathologic change in the peritoneal tissue, named appropriately "wet" and "dry," have been recognized and described.[9] It is to be remembered, however, that these forms are not distinct entities, but overlap somewhat, so that both forms may occur simultaneously in different portions of the same abdomen.

Wet, or exudative, peritonitis usually occurs in the early stages of the disease. The peritoneal surfaces are covered with numerous small miliary tubercles, which are also scattered over all the organs. Each tubercle is surrounded by an area of inflammation and serous exudation. These areas of exudation give rise to an accumulation of fluid, often enormous in amount. In addition to these changes the omentum may be infiltrated and thickened, frequently with the formation of hard masses.

In dry, or adhesive, peritonitis, exudation is at a minimum. Fibrin forms between the visceral and the parietal layer of the peritoneum and even between the visceral layers of the peritoneum. Boyd [10] has shown by selective staining that this interlayer is fibrin rather than fibrous tissue. The end result of this process is a solid matting together of the abdominal viscera. It is this biologic response, the walling off of the infection, that makes a roentgen diagnosis possible.

Chronic tuberculous peritonitis, therefore, may develop by any one of three routes: (1) perforation, (2) lymphatic channels or (3) the blood stream. The relation between tuberculous peritonitis and tuberculous salpingitis is not clearcut. Some investigators have stated the belief that in the female the fallopian tubes are the most frequent source of infection [11]; others have expressed the opinion that the tubes are secondarily rather than primarily involved.[7b] Since the sex incidence of tuberculous peritonitis is about equal, it seems illogical to consider the fallopian tubes as a primary source of the infection.[12]

9. Van Antwerp, L. D.: Tuberculous Peritonitis in Children, New England J. Med. **217**:995-998, 1937. Blake.[1a] Boyd and MacCallum.[7]

10. Boyd, W.: Tuberculous Peritonitis, in Surgical Pathology, Philadelphia, W. B. Saunders Company, 1942, pp. 364-366.

11. Hertzler, A. E.: Diseases of Peritoneum, in Christopher, F.: Major Surgery, Philadelphia, W. B. Saunders Company, 1943, pp. 1071-1072. Boyd (footnotes 7*a* and 10).

12. Olcott, C. T., and Paccione, D.: Tuberculous Peritonitis, Am. Rev. Tuberc. **28**:27-61, 1933.

INCIDENCE, AGE AND RACE

The incidence of tuberculous peritonitis will vary according to the type of institution in which the study is made. At the Massachusetts General Hospital in the past five years only 17 cases were found in a total of 182,329 admissions. In 14 the diagnosis was made on the basis of observations made by biopsy, smear, culture or guinea pig inoculation; in the remaining 3 it was made on clinical grounds alone. Bircher [13] in 1907, in reviewing reports of 14,000 autopsies collected from the literature, found an incidence of 3.5 per cent. Olcott and Paccione [12] in 1938 reported 109 cases of tuberculous peritonitis (0.13 per cent) in a total of 65,000 admissions to the New York Hospital. Undoubtedly in an institution devoted to the care of tuberculous patients the incidence of tuberculous peritonitis would be higher than in a general hospital.

The age of the patient is of clinical significance. Children and young persons are most frequently affected. All writers agree, however, that tuberculous peritonitis may occur at any time during the life span.

The relation of race to incidence is difficult to evaluate. Reports that Italians [14] and Negroes [15] are particularly susceptible are unsubstantiated, since such reports ignore the socioeconomic factors, which are probably more vital in determining susceptibility than race.

CLINICAL MANIFESTATIONS

The protean manifestations of tuberculous peritonitis can be appreciated from the classic description of Pincoffs and Boggs.[1b] Ascites, usually insidious and painless in its onset, is almost always present at some stage of the disease and is due to the rapid formation of tubercles over the peritoneal surface. Consequently it is more common in the early stages and will recur when chronic caseous tubercles break down and further extension of the disease occurs. A wide variation in the symptoms in the gastrointestinal tract exists, and none or many may occur. Abdominal pain, loss of appetite, occasional nausea and vomiting, slight constipation, and a sensation of fulness in the abdomen are the most frequent complaints. The pain may vary in its location and its severity, but all authorities have stressed the mildness of the symptoms. A low grade fever

13. Bircher, E.: Die chronische Bauchfelltuberculose: Ihre Behandlung mit Roentgenstrahlen, Inaug. Dissert., Aarau, G. Keller, 1907; cited by Olcott and Paccione.[12]

14. Cabot, R. C.: Differential Diagnosis, Philadelphia, W. B. Saunders Company, 1914, vol. 2, p. 103. Olcott and Paccione.[12]

15. Barrow, D. W.: Tuberculous Peritonitis, South. M. J. **36**:646-650, 1943.

with daily elevations of temperature and occasional chills is an almost constant finding. The white blood cell count may be slightly elevated, but as a rule it is within the normal range.[12]

Physical examination will usually reveal a thin, emaciated person in the younger age group, with a distended abdomen. Soft doughy masses may be palpable within the abdomen; these are due to infiltration and thickening of the omentum and its contraction into lumps by the formation of adhesions.[10]

Tuberculosis elsewhere is not a constant feature. In 18 of 109 cases, Olcott and Paccione [12] found at autopsy no infection outside the peritoneal cavity; in the remaining cases tuberculosis was found, in order of frequency, in the intestines, the fallopian tubes and the lungs. Barrow [13] found clinically that only 1 of 5 patients had active tuberculosis elsewhere. In the 6 cases presented here no active tuberculosis was found except in the peritoneum.

ROENTGEN FINDINGS

In the wet form of tuberculous peritonitis the plain roentgenogram taken in an early stage of the disease usually shows ascites with a low grade ileus. The characteristics of abdominal ascites have been well described by Laurell [16] and others.[17] A diffuse haziness of the abdomen is seen, with obliteration of the outlines of the psoas muscles and the subperitoneal fat. The small intestine, which is usually filled with gas, appears to be floating free in the abdomen. The diaphragm is elevated. These features are not distinctive and may occur in a number of other diseases which are characterized by an accumulation of peritoneal fluid. However, the presence of ascites in a young person, with a history of onset several weeks or months before, should suggest the possibility of tuberculous peritonitis, and further study of the colon and the small bowel should be undertaken.

In the dry form of tuberculous peritonitis the scout film demonstrates ileus alone. Here again there are no pathognomonic signs. The small intestine is drawn up high in the abdomen, but this position is difficult, in fact almost impossible, to determine without the aid of a contrast substance.

A roentgenoscopic and roentgenographic examination of the colon after a barium sulfate enema is more informative. In my cases it revealed no intrinsic lesions, but the possibility of tuberculosis of the ileocecal region should always be borne in mind, as it may be the origin of tuberculous peritonitis. In tuberculous peritonitis the intestinal wall is rigid, with areas of narrowing and areas of dilatation, and the bowel is not freely movable in the peritoneal cavity. These features are present even in the wet form, because the two forms overlap and some degree of adhesive peritonitis is present in all cases. Roentgenograms taken after evacuation of the barium sulfate will confirm this impression. If the intestine is normal a completely empty transverse colon will tend to occupy a position lower in the abdomen than it did when the distending mass of barium sulfate was present within its lumen. In tuberculous peritonitis there is little or no change in the position of the transverse colon after evacuation of barium sulfate. Also on the film taken after the barium has been evacuated adhesive bands retracting the intestinal wall may sometimes be seen.

Of greatest value is the study of the small bowel, which may be made by serial films or by injecting a barium sulfate mixture directly into the small bowel, after the method of Schatzki.[4] The first abnormality noted is the rapid passage of barium through the small bowel, only about six minutes being required for its transit. A cause for this rapid movement of barium is that peritoneal irritation results in spasm of the muscularis mucosae, as explained by Golden.[18] Rigidity and fixation of the loops of small intestine are marked, and extended observation will show no change in their position. The small intestine is shorter, and it occupies a smaller space than normal. Pincoffs and Boggs [1b] observed at postmortem examination that the small intestine is frequently pulled to the right. My studies did not confirm this point but did demonstrate displacement upward as a rule. Occasionally a few loops may be low down in the pelvis, particularly in female patients with accompanying tuberculous salpingitis. Although the small intestine is matted together, the intervening spaces between the barium-filled loops of small bowel are slightly widened and irregular, owing to the interspersion of fluid and fibrin between the peritoneal surfaces. No definite arrangement of the loops of small bowel was noted, other than that they were irregular and bizarre, as observed also by Ritvo [2] and Soper.[3] Abnormal segmentation of the barium-filled bowel, indicating a disturbance in intestinal motility, was seen in 3 of my patients.

16. Laurell, H.: Roentgenologic Signs of Abdominal Effusion: Roentgen Diagnosis of Peritonitis, Acta radiol. **5**:63-104, 1926; A Contribution to the Roentgenological Differential Diagnosis in the Presence of Free Fluid in the Abdomen, ibid. **16**:424-425, 1935.

17. Cosacesco, A.; David, N., and Stanesco, C.: Roentgen Image of Free Intraperitoneal Fluid in Peritonitis, Presse méd. **27-28**:310-312, 1940.

18. Golden, R.: Disturbances in Small Intestinal Motility, paper read at the meeting of the New England Roentgen Ray Society, May 19, 1944.

DIFFERENTIAL DIAGNOSIS

The diagnostic points which I have enumerated are fairly conclusive for a generalized chronic adhesive process in the peritoneum. Several diseases other than tuberculous peritonitis may give a somewhat similar roentgenographic appearance and should be considered in establishing the diagnosis.

Adhesive peritonitis with ascites will occur with carcinomatous peritonitis. This is frequently secondary to carcinoma in the gastrointestinal tract or in the female genital organs. A primary malignant growth in the gastrointestinal tract will be demonstrated with the routine barium sulfate enema, and the bimanual pelvic examination should disclose malignant disease of the lower part of the genital tract. In ovarian carcinoma, which usually occurs in persons in an older age group, a mass in the pelvis may be seen clearly, displacing the viscera upward. On the other hand, in tuberculous salpingitis, when it accompanies peritonitis, the pelvic mass tends to bind down the lower loop of ileum. Lymphoma of the intestine with involvement of mesenteric lymph nodes is generally more localized. The finding of disease elsewhere in the body will aid in the differential diagnosis. Theoretically, primary colloid carcinoma of the peritoneum would be impossible to distinguish from chronic tuberculous peritonitis. Unfortunately no case of this disease was available for this study.

In ovarian or paraovarian cyst a large mass will be visible, displacing the viscera upward. The adhesive factors, however, are absent. Retroperitoneal hernia of the bowel might cause the segments of intestine to be drawn together but would not cause change in motility.

Other diseases which will produce ascites should be considered, including heart disease, cirrhosis or cancer of the liver, renal disease and pyeloplebitis, but the clinical features and the chemical picture of the blood will be different. Roentgenologically the signs of adhesion in the large and small bowel will be absent.

REPORT OF CASES

CASE 1.—The changes in the small intestine were noted on review of the roentgenograms, after the diagnosis had been established by exploratory laparotomy and biopsy. This case was reported by Schatzki.[4] It is presented here in greater detail, since it initiated subsequent investigation of tuberculous peritonitis.

V. R., a 48 year old Polish man, was admitted to the hospital in November 1942, with the complaint of loss of weight and abdominal pain of four months' duration.

History.—The patient suffered with vague abdominal pain midway between the xiphoid process and the umbilicus, occasional nausea but no vomiting. He had lost 20 pounds (9 Kg.) in three months; there was no evidence of diarrhea or tarry, bloody or clay-colored stools. He had been inconvenienced by nocturia (urinating twice nightly) for several years, but there were no other urinary symptoms.

Physical Examination.—The patient was a well developed man, showing evidence of recent loss of weight, but he was in no acute distress. His skin was dry and hanging in folds; he had a few carious teeth. His pulse was regular, and his blood pressure was 165 systolic and 102 diastolic; his heart was not enlarged to percussion. The abdomen was tense, with a questionable mass in the right lower quadrant; there was gaseous distention. The right lobe of the prostate was harder than normal but not enlarged. His temperature while he was in the hospital varied between 98 and 100 F., reaching 104 on one occasion.

Laboratory Examination.—The urine was normal. Examination of the blood revealed a hemoglobin content of 74 per cent, 4,500,000 red cells and 10,300 white cells, with polymorphonuclear cells 64 per cent, lymphocytes 28 per cent and monocytes 8 per cent. The stool gave a negative reaction to the guaiac test. Chemical examination of the blood showed sugar 82 mg. per hundred cubic centimeters, and nonprotein nitrogen 22 mg., chlorides 96.9 mg. per liter, carbon dioxide 26.8 mg. per liter, albumin 1.8 Gm. and globulin 7.3 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 0.25. The prothrombin time was thirty-one seconds (normal was twenty-seven seconds). The reaction of the blood to a Hinton test was negative.

Roentgen Examination.—A roentgenogram of the chest showed linear areas of atelectasis above the diaphragm on both sides, but it was otherwise normal. A series of roentgenograms of the gastrointestinal tract, and films taken after an enema of the small intestine and a colonic enema gave negative results.

Exploratory Operation (Dec. 8, 1944).—The peritoneum was tremendously thickened, as if involved in a chronic process, and there were many small white spots on it of a type that could be associated with chronic tuberculosis. Histologic study of a surgical specimen revealed caseous tuberculosis.

In view of the pathologic diagnosis, the films taken after an enema of the small intestine were reviewed, and several suggestive factors became apparent. The small intestine filled easily; the intestinal loops were grouped with too great regularity, and the length of the small intestine was perhaps unduly short. The lower border of the small intestine appeared somewhat smooth and higher than usual. No intrinsic lesion, however, was evident. The combination of these findings should have indicated chronic intraperitoneal disease, such as tuberculous peritonitis.

CASE 2.—The diagnosis was suggested by the roentgenographic appearance of the large bowel and was substantiated by serial films of the small bowel taken hourly. The roentgenologic diagnosis was confirmed by peritoneoscopy and biopsy.

T. G., a 45 year old Syrian man, was admitted to the hospital in January 1944, with a complaint of a heavy sensation in the epigastrium of two months' duration, unassociated with pain or gas.

History.—The patient suffered with epigastric distress, consisting of a continuous sensation of heaviness, which was worse after meals, unaccompanied by sharp

pain, nausea or gas. Vomiting had occurred on a few occasions. His appetite had been poor, and the patient had lost 22 pounds (10 Kg.) in weight. For two months, sweats and chills during night and morning plus a continuous feverish feeling had also been present. Constipation, which required the continuous use of laxatives and which had been present for five or six years, had recently become worse. Fatigue occurred more easily than formerly.

Physical Examination.—There was evidence of loss of weight; the nasal septum was deviated, and the teeth were carious. Tenderness to deep pressure in the epigastrium and muscle spasm were found. No masses could be felt, but the spleen and the liver were both palpable. His temperature during the stay in the hospital ranged from 98 to 104 F.

Laboratory Examination.—The urine was normal. Examination of the blood showed 5,400,000 red cells, 6,500 white cells and a hemoglobin content of 12 Gm. per hundred cubic centimeters. A hemogram showed polymorphonuclear cells 71 per cent, lymphocytes 24 per cent and monocytes 5 per cent. Serologic reactions to a Hinton and a Widal test and to a test for undulant fever were negative. The stool gave a negative reaction to the guaiac test.

Roentgen Examination.—A roentgenogram of the chest was essentially normal. A series of roentgenograms of the gastrointestinal tract showed no definite intrinsic disease in the esophagus, the stomach or the duodenum. A barium sulfate enema was given on Jan. 18, 1944. The colon filled readily, without evidence of obstruction. The sigmoid colon was high, and the splenic flexure was displaced medially. The cecum could not be entirely filled, but no abnormality was demonstrated. The terminal portion of the ileum appeared normal. After evacuation of the barium sulfate the mucosal pattern was normal, but there appeared to be an abnormal rigidity of the colon. There was no change in its position following evacuation. The possibility of diffuse adhesions resulting from tuberculous peritonitis was suggested. An enema of the small intestine was given Jan. 31, 1944. Hourly films showed the loops of the small bowel to be in an extremely fixed position but otherwise not remarkable. The findings were consistent with tuberculous peritonitis (fig. 1).

Peritoneoscopy (Jan. 24, 1944).—Multiple adhesions were present, which prevented visualization of the spleen or the liver. On the peritoneal surfaces of the adhesions and on parts of the bowel, which were unrecognizable, there were numerous tubercles, 1 to 3 mm. in diameter. Biopsy revealed tuberculosis of the peritoneum.

CASE 3.—The clinical diagnoses considered in this case were ulcerative colitis, diverticulitis, carcinoma of the colon and tuberculous peritonitis. The first three were excluded by careful study of the colon and small bowel, while the changes found seemed consistent with tuberculous peritonitis. Subsequent peritoneoscopy and biopsy confirmed this diagnosis.

A. Le R., a 47 year old man, was admitted to the hospital in April 1944, complaining of generalized abdominal distress of two months' duration.

History.—The patient, a physician in a tuberculosis sanatorium, had had pulmonary tuberculosis, which had been inactive for many years. He was well until two months before admission to the hospital, when he began to suffer from generalized, vague abdominal distress associated with constipation. He lost his appetite and some weight but had had no bloody or tarry stools, nausea or vomiting. For four weeks before entry to the hospital he had fever every afternoon; three weeks before his admission a localized cramplike pain in the left lower abdominal quadrant lasting an hour and recurring for a week, appeared. There had been some symptomatic improvement in the two weeks before he was admitted. A roentgenogram of the chest taken at his own hospital had shown no evidence of active tuberculosis; a barium sulfate enema had revealed some rigidity of the descending colon on the left side.

Physical Examination.—The patient was a well developed man, not in acute distress. His blood pressure was 130 systolic and 70 diastolic. His abdomen was distended, but there was no definite tenderness or spasm; peristalsis was not hyperactive. There was questionable shifting dulness; no masses were felt. Examination of the chest revealed generalized wheezing, which was

Fig. 1 (case 2).—Roentgenograms taken after a barium sulfate enema, before (*A*) and after (*B*) evacuation. There has been no change in the position of the colon after it was relieved of the weight of the barium sulfate and the patient assumed the upright position, indicating that a diffuse, adhesive process prevents motion of the colon and its mesentery.

especially prominent in the upper part of the lungs, with fine moist inspiratory rales in the apexes. In the hospital, his temperature ranged between 98.6 and 101 F.; his pulse rate varied between 90 and 120.

Laboratory Examination.—The urine contained albumin (2 plus) and a sediment, which consisted of 5 red blood cells, 1 white blood cell and 3 epithelial cells per high power field and mucin, with occasional clumps. Studies of the blood showed 4,000,000 red cells, 13,500 white cells and a hemoglobin content of 11 Gm. per hundred cubic centimeters. A hemogram showed polymorphonuclear cells 75 per cent, lymphocytes 14 per cent, monocytes 10 per cent, eosinophils 1 per cent and a rare polychromatophil. There was moderate achromia, with moderate variation in the size of the red cells and normal platelets. The stool was yellow and liquid and gave a negative reaction to the guaiac test. The serologic reaction to a Hinton test was negative. The sedimentation rate of the red cells was 15, 30, 44 and 48 mm. per hour. In a sulfobromophthalein sodium test (5 mg. per kilogram) 40 per cent of the dye was excreted in forty-five minutes. A cephalin-cholesterol flocculation test gave a negative result.

Roentgen Examination.—At least two roentgenograms, which were taken at another hospital, showed the lower part of the small bowel to be fixed in position. A barium sulfate enema was given on April 26, 1944. Barium sulfate passed from the rectum to the cecum without delay. There was reflux into a normal-appearing terminal portion of the ileum. The lumen of the upper half of the rectum appeared slightly narrower than usual and the distance between the posterior rectal wall and the sacrum greater, but there was no evidence of intrinsic defect in the upper part of the rectum or sigmoid. The midsigmoid appeared kinked on itself, and its relationship to the remainder of the sigmoid could not be changed by palpation; this suggested that it was fixed in position by extrinsic adhesions. No definite filling defect, ulceration or diverticula could be seen in the colon. Indistinct peritoneal markings indicated moderate ascites. Because the findings suggested tuberculous peritonitis, study of the small bowel was recommended.

A small intestinal enema was given on April 27, 1944. Barium sulfate flowed at a normal rate from the duodenal loop to the jejunoileal junction. The mucosal relief of the jejunum was normal, and its loops were freely movable on palpation. All of the small bowel, however, lay above the level of the pelvis. At the end of four minutes barium sulfate began to regurgitate into the stomach, and no progression into the small bowel was demonstrated for the next ten minutes, during which time a total of 1,200 cc. of barium sulfate solution was injected. Roentgenograms taken immediately after the enema showed beginning passage of the barium sulfate into the ileum, and one-half hour later it had reached the cecum. No dilated loops were apparent, and so far as could be seen the filled loops of bowel were freely movable in relation to one another. The small intestine was at all times high in position, however, and never descended below the crest of the ilium on the left side or went into the true pelvis on either side. The general configuration of the small bowel had not changed since the examinations made elsewhere one month before. The position of the small bowel was abnormal and consistent with old peritonitis (fig. 2). An electrocardiogram showed no evidence of pericarditis; proctoscopy gave essentially negative results except for some spasm in the rectum.

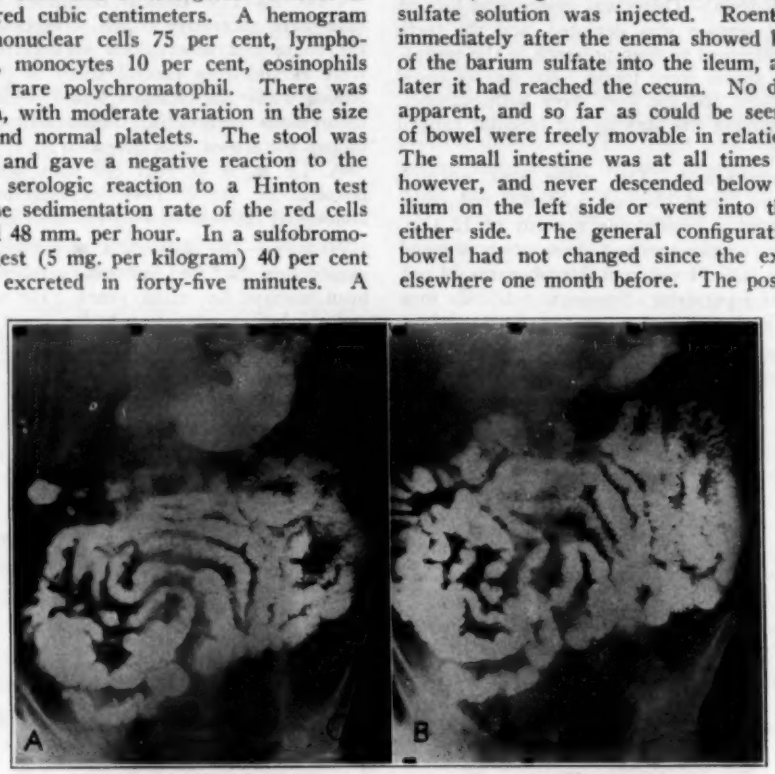

Fig. 2 (case 3).—Roentgenograms taken one-half hour (*A*) and one hour (*B*) after an enema of the small intestine. Although the individual loops of small bowel are movable, the entire small intestine is elevated. It can be seen that this is not caused by a pelvic tumor. The general configuration of the small bowel remains enlarged.

Peritoneoscopy (May 2, 1944).—A small amount of fluid was demonstrable in the right lower quadrant of the abdomen, only a few drops of which could be aspirated. The peritoneal surfaces throughout were slightly reddened and presented numerous white pinpoint tubercles typical of those in tuberculous peritonitis. These were present on the round ligament of the liver, on the small bowel and on the peritoneum of the abdominal wall. The liver appeared normal. Histologic studies revealed no diagnostic abnormality of the liver and tuberculosis of the peritoneum.

Case 4.—This patient was from another hospital, where an exploratory laparotomy and biopsy had been done. Owing to the unavoidable lag in the transmission of records the patient was fully studied before the history and slides were received. The diagnosis was made on the basis of the changes in the large bowel and was substantiated later by the surgeon's report

and the microscopic sections, which were reviewed by the pathologist at the Massachusetts General Hospital.

History.—P. M., a 16 year old single Turkish girl, was admitted to the hospital in April 1944, complaining of chills and fever of one year's duration. She had had no known contact with tuberculosis. One year before admission to the hospital she had noted fatigue and a run-down feeling, which one week later were followed by daily nausea and vomiting, chills and fever. The nausea and the vomiting subsided at the end of a week with treatment at the hospital, but chills, fever, anorexia and fatigue continued, in spite of rest in bed. After an exploratory laparotomy she spent six months in a sanatorium, without improvement.

Physical Examination.—The patient was an underdeveloped or undernourished, tired-looking girl who appeared chronically ill. Her pulse rate was 110 and her blood pressure was 90 systolic and 70 diastolic. There was tenderness over the right side of the epigastrium in the region of the operative scar. Her temperature on admission to the hospital was 101 F., ranging throughout hospitalization between 99 and 104.5 F. (practically sustained fever with a rare normal temperature). Her pulse rate was from 80 to 130, averaging 100; her respiratory rate was from 20 to 35.

Laboratory Examination.—The urine was normal. Examination of the blood revealed 4,200,000 red cells, 21,200 white cells and a hemoglobin content of 12 Gm. per hundred cubic centimeters. A hemogram showed polymorphonuclear cells 79 per cent, lymphocytes 14 per cent, monocytes 3 per cent, a few toxic polymorphonuclear cells, no malaria organisms, myelocytes, 4 per cent and a few target cells. A smear was normal. The sputum was thick and mucoid gray and contained no tubercle bacilli. Both the sputum and the stool gave negative reactions to a guaiac test. The gastric juice contained no tubercle bacilli and no free acid; there was 1 unit of acid after administration of histamine. A nasal smear failed to reveal tubercle bacilli. The reaction to tuberculin in a 1:10,000 dilution was strongly positive.

Roentgen Examination (April 17, 1944).—Roentgenograms showed enlargement of the spleen, with the liver within the upper limits of normal. An intravenous pyelogram showed no abnormalities. A roentgenogram of the chest showed calcification in the base of the upper lobe of the right lung and a calcified gland in the mediastinum. There was no definite evidence of active disease within the pulmonary fields. A roentgenogram of the abdomen indicated that the bones of the pelvis were somewhat atypical.

A barium sulfate enema was given on April 20, 1944. Barium sulfate flowed readily to the cecum, and the entire colon filled well. The ileocecal valve opened, and a long loop of ileum in the terminal portion filled and appeared normal. The film taken after evacuation showed good emptying and a normal colon. There were, however, numerous loops of nondilated small bowel on the right side of the abdomen.

A roentgenographic series of the gastrointestinal tract on April 26, 1944 showed that the esophagus was normal, that the stomach contained considerable secretion, which obscured the details of the gastric mucosa, and that there was a small residue of the motor test meal. The pylorus opened after a slight delay; the duodenal cap was deformed. On the greater curvature was a crater, approximately 2.5 cm. distal to the pylorus and slightly toward the anterior wall. The crater measured 5 mm. The remainder of the duodenal loop appeared normal. The residue of the motor meal was in the terminal portion of the ileum and the proximal part of the colon (fig. 3).

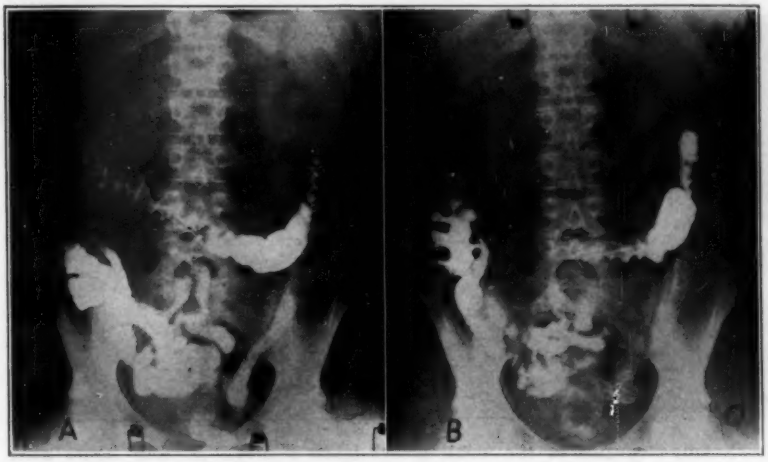

Fig. 3 (case 4).—Two roentgenograms of the same patient taken one week apart, each after evacuation of a barium sulfate enema. Comparison of *A* and *B* shows that there has been only a slight change in the position of the colon and the terminal portion of the ileum. The configuration of the terminal portion is abnormal, suggesting a matting together of the loops.

Another barium sulfate enema was given April 28, 1944. The results were normal except for slight irritability in the cecum and the ascending colon, which were filled and appeared normal. After the results of the two examinations were compared the conclusion was that it was unusual for the colon and the demonstrated portion of the lower part of the small intestine to remain in the same position. This suggested a lack of flexibility and changes similar to those in dry tuberculous peritonitis.

Microscopic sections from another hospital were received and reviewed on April 29, 1944. There was histologic evidence of tuberculosis.

CASE 5.—This patient was seen some years before the present study was begun. The case is included because the roentgenologic changes were extensive,

although their full diagnostic significance was not realized at the time. Study of the small bowel was repeated in 1944 by passing the barium mixture through a Miller-Abbott tube, and the matting together of the small bowel persisted. The diagnosis was made by exploratory laparotomy and biopsy; it might have been made on the basis of the roentgenographic appearance of the small bowel.

A. K., a 38 year old married woman, was admitted to the hospital in March 1940, because of abdominal pain of seven months' duration.

History.—She had been in the hospital for one week in October 1936, at which time she was discharged with the diagnosis of "abdominal pain of undetermined origin, calcified abdominal glands and question of old tuberculous peritonitis." She was fairly well between 1936 and 1940 but continued to have recurrent, moderate attacks of pain in the right lower quadrant of the abdomen, at times radiating down the anterior surface of the right leg. In August 1939, a colicky, midhypogastric pain appeared; in October she was confined to bed for a month because of abdominal pain, and 80 diastolic; her temperature was normal and her pulse rate 80 to 100.

Laboratory Examination.—The urine was normal. Studies on the blood revealed 4,040,000 red blood cells, 9,400 white blood cells, a hemoglobin content of 77 per cent, polymorphonuclear cells 60 per cent, lymphocytes 30 per cent, monocytes 9 per cent and eosinophils 1 per cent. A smear was normal. The stool was light gray and liquid and gave a negative reaction to the guaiac test. The Hinton test gave a negative result. The reaction to the van den Bergh test was normal; the blood protein content was 6.6 per cent and the nonprotein nitrogen 18 mg. per hundred cubic centimeters.

Roentgen Examination.—A plain roentgenogram of the abdomen revealed multiple areas of calcification in the lower part of the abdomen, which were probably calcified glands. There were several slightly dilated loops of small intestine in the left upper abdominal quadrant and a small amount of gas in the large intestine. A barium sulfate enema was given March 6, 1940. The enema indicated probable calcified glands and extrinsic pressure in the region of the sigmoid. Serial

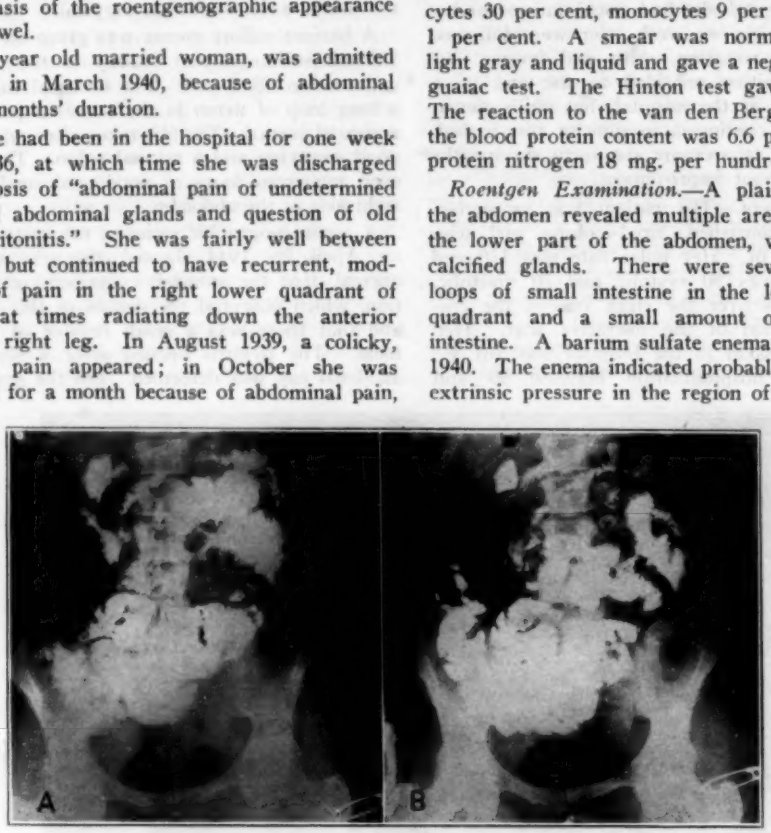

Fig. 4 (case 5).—Roentgenograms of the small bowel taken hourly. *A,* four hours after administration of barium sulfate. *B,* five hours after administration of barium sulfate. The small intestine is drawn into the abdomen and matted together, owing to the diffuse adhesive process. Slight widening and irregularity of the spaces between the loops of intestine can be seen.

associated with chills and intermittent sweats. During the last two weeks of this illness she became jaundiced and the stools were clay colored; the pain shifted in location, occasionally radiating to the angle of the right scapula. One week before entry to the hospital the stools were again light colored, but she was not jaundiced. There had been no vomiting, diarrhea or tarry stools, although when she was constipated the stools had at times been flecked with blood. There had been no loss of weight.

Physical Examination.—The patient was fairly well developed and nourished and not in acute distress. Her tongue was pale, as were her hands, which had a peculiar cyanotic appearance in the fingers. The abdomen was slightly distended; there was hyperperistalsis; palpation was difficult, owing to resistance of the abdomen. The liver and the spleen were not felt; there was slight tenderness in the right upper quadrant of the abdomen. Pelvic examination showed a poorly defined mass in the left lower abdominal quadrant, the size of a hen's egg, apparently connected with the fundus and occupying the position of the left ovary. The blood pressure was 120 systolic

roentgenograms of the small intestine on March 11, 1940 showed no delay in the passage of barium. The jejunal loops showed some dilatation, which changed in degree during the examination. The ileum was not dilated. Its loops stayed together in a rather peculiar constant arrangement, as if they were in some kind of sac. There was definite abnormality in the small intestine, which was considered to be due to an underlying peritoneal lesion. A second examination confirmed the partial obstruction, but it was still a question whether adhesions had produced the abnormalities (fig. 4).

Exploratory Laparotomy (March 27, 1940).—No free peritoneal cavity could be demonstrated. The abdomen looked as if glue had been poured into it and had stiffened it to a tough fibrous consistency, which bound adjacent coils of intestine together. These adhesions formed septums, or compartments. A piece of one of them was isolated for biopsy. There was histologic evidence of tuberculosis.

CASE 6.—This case indicates that changes in the peritoneal cavity will persist for some time after apparent subsidence of disease.

A. S., a 35 year old Negro woman, was admitted to the hospital in May 1944, because of syphilis of the central nervous system.

History.—Three years before admission to the Massachusetts General Hospital she was treated in another hospital for chronic tuberculous peritonitis, proved by aspiration and guinea pig inoculation. On admission to the Massachusetts General Hospital she complained of vague pain in the abdomen and occasional nausea but no vomiting. This patient was studied because of interest in determining how long roentgen changes attributable to tuberculous peritonitis persist, although the patient becomes relatively asymptomatic.

The results of laboratory tests, the temperature, the pulse and the respiratory rate were normal.

Roentgen Examination.—A roentgenogram of the chest was essentially normal. A small intestinal enema was given May 23, 1944. Barium sulfate passed through the small intestine rapidly, reaching the cecum in five or six minutes. The length of the small intestine was less than normal, and there was some fixation of the loops. The space between the individual loops, however, was widened. At the end of three hours the greater part of the barium sulfate had passed into the colon. There was some abnormal segmentation of the small bowel. The findings suggested adhesive peritonitis, probably tuberculous in origin. A barium sulfate enema showed a normal large bowel.

SUMMARY

Six cases of tuberculous peritonitis are presented in 3 of which the preoperative diagnosis was suggested by the roentgenographic appearance of the large and the small bowel.

Tuberculous peritonitis results in a diffuse adhesive process involving the peritoneal surfaces. This gives rise to certain distinctive features, which may be seen on the plain roentgenogram and on roentgenograms of the large and small intestines taken after barium sulfate enemas. These diagnostic points are:

1. A low grade ileus with a varying amount of intra-abdominal fluid will be seen on the plain roentgenogram.

2. The barium sulfate enema will show the large bowel to be in a fixed position. Occasionally adhesions can be demonstrated.

3. The enema of the small intestine will disclose rapid passage of the barium sulfate as a rule. The loops of the intestine are bound together, and the bowel is shorter than normal. The intervening spaces between the barium-filled loops tend to be slightly widened and irregular. Abnormal segmentation may be seen.

EFFECT OF MASSIVE EXPERIMENTAL HEMORRHAGE ON HEPATIC FUNCTION IN DOGS

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Little can be found in the literature at the present time, from either the experimental or the clinical standpoint, to indicate what effect massive hemorrhage followed by shock might have on hepatic function. Since the liver is important for the synthesis of certain blood proteins, including fibrinogen, and since severe hemorrhage can considerably deplete these proteins, impaired hepatic function produced by hemorrhage might result in inadequate restoration. It is possible that other functions of the liver also might be decreased as a result of hepatic cellular damage due to hemorrhage. Patients who die of severe postoperative shock caused by hemorrhage present clinical manifestations similar to those observed in so-called "liver death," which has been described in detail by Boyce and McFetridge [1] and others. However, it is well established that most of the patients with manifestations of "liver death" have had definite impairment of hepatic function due to previous hepatic infection or damage and perhaps have had a preoperative hepatic function which was at or below the critical level. It has not been established as yet that severe hemorrhage causes enough hepatic damage to be of any significance.

The experimental work to be presented was performed in an effort to determine whether or not massive hemorrhage could produce enough damage to the liver to give rise to hepatic insufficiency. The work of Blalock [2] and of others has sufficiently proved that shock per se and shock due to hemorrhage are two separate and distinct clinical entities, although similar in many respects. The former is identified by hemoconcentration and definite pathologic changes in the organs which are observed at necropsy and is characterized by diffuse edema and focal necroses in the liver, kidneys and other organs. The typical picture seen at necropsy after death due to hemorrhage, in contradistinction, consists of hemodilution and normal organs except for their pallor and shrunken appearance.

DeLor and Reinhart,[3] in their analysis of tests of hepatic function in 381 cases, found that the sulfobromophthalein (bromsulphalein) test, the blood prothrombin test and the hippuric acid test gave roughly parallel results as hepatic function was diminished. The galactose tolerance test was the least reliable. The sulfobromophthalein test was the most sensitive for the identification of early hepatic damage. The mortality rate mounted rapidly for persons with 50 per cent or more diminution of hepatic function, as estimated by these tests. DeLor and Reinhart concluded that if results of two or more of the tests indicate diminished hepatic function the mortality and the morbidity rate are definitely greater and that as yet no single test of hepatic function furnishes as reliable a prognosis as that which may be derived from two or more tests.

Rhoads and Warren [4] studied the prothrombin content of the plasma in persons with hepatic injury and also in completely hepatectomized dogs and stated that the liver is probably the sole source of synthesis of prothrombin. Smith and co-workers,[5] in recent work in their laboratory, showed that the liver is important in the manufacture of prothrombin. Ordinary tests for determining bleeding and clotting time reveal an abnormality only when prothrombin deficiency is extreme. They give normal results even when the plasma prothrombin value is approaching the danger level. Smith and associates have found by their bedside technic that a tendency to bleeding commonly occurs when the test gives values of 40 per cent or less. Values of 40 to 70 per cent are definitely in the danger zone. They also noted that for laboratory workers the normal variations in the prothrombin time are rarely more than 15 per cent of normal.

From the Department of Surgery, University of Illinois College of Medicine, and the Research and Educational Hospital.

1. Boyce, F. F., and McFetridge, E. M.: So-Called "Liver Death": Clinical and Experimental Study, Arch. Surg. **31**:105 (July) 1935.

2. Blalock, A.: S. Clin. North America **21**:1661-1683 (Dec.) 1941.

3. DeLor, J., and Reinhart, H. L.: Am. J. Clin. Path. **10**:617 (Sept.) 1940.

4. Warren, R., and Rhoads, J. E.: Am. J. M. Sc. **198**:193 (Aug.) 1939.

5. Smith, H. P.; Ziffren, S. E.; Owen, C. A., and Hoffman, G. R.: Am. J. Clin. Path., Tech. Supp. **4**: 13 (Jan.) 1940.

Price, Hanlon, Longmire and Metcalf,[6] in their experiments on the effects of acute hemorrhage in healthy dogs reported no specific data regarding the effects on hepatic function in the animals in their series. The amount of blood which they removed per animal averaged 35.8 cc. per kilogram of body weight. The amount of blood removed from animals in our series to produce massive experimental hemorrhage was only 30 cc. per kilogram. However, the bleeding time for our experiments, being only thirty minutes, was much shorter than that used by Price and co-workers.

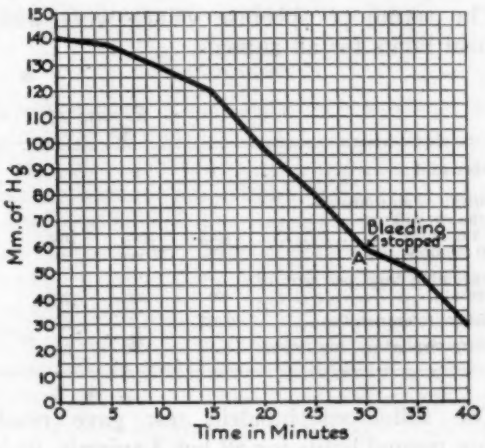
Moon and associates[7] suggested that for the sake of accuracy the expression "shock and hemorrhage" should be substituted for the term "hemorrhagic shock." They urged investigators not to use hemorrhage as a means of producing shock experimentally. If the results so obtained are interpreted as applying to shock, erroneous conclusions may be drawn. Harkins[8] stated that his work and that of Blalock and of others have led to a conclusion contrary to that of Moon, namely, that if the hemorrhage is allowed to continue long enough the restitution of even more blood than was lost will not restore the animal or the patient.

EXPERIMENTAL TECHNIC

In an attempt to simulate as closely as possible conditions of hemorrhage as they would occur in the operating room, dogs, under anesthesia induced with intravenously administered pentobarbital sodium, were bled from the jugular vein, predetermined amounts of blood being taken every five minutes for from thirty to thirty-five minutes. Previous experimental work has shown that if blood in the amount of 0.5 per cent of body weight is withdrawn every five minutes for thirty minutes the blood pressure drops below the critical level and death invariably ensues within ten minutes unless supportive therapy is given immediately on cessation of the bleeding.

The accompanying graph represents the mean blood pressure readings for many experimental animals. If, for example, blood equal to 0.5 per cent of the weight of a dog weighing 15 Kg., or 75 cc., was withdrawn every five minutes for thirty minutes, 525 cc. of blood would be removed. This corresponds to approximately 3 per cent of the body weight. Bleeding was terminated at this point, designated by *A* on the graph. The mean blood pressure, indicated by *A*, was 58 mm. of mercury. The blood pressure readings were checked both by a cannula in the femoral artery and by a cuff on the leg. However, the criterion used to determine the end point of the bleeding was not the blood pressure but the calculated total amount of blood. Obviously with this method several animals died before our bleeding technic became sufficiently accurate to bleed the animals to the minimum level compatible with life. A total of 12 animals were bled in this manner. Four animals had to be given transfusions of from 2 to 3 ounces (60 to 90 cc.) of their own blood in order to keep them alive. One animal died within the first twelve hours, apparently from hemorrhage.

The 11 animals that survived were subjected to tests of hepatic function at varying intervals postoperatively for ten days. The tests used were the sulfobromophthalein sodium (bromsulphalein) test, as described by Rosenthal and White,[9] the galactose tolerance test, introduced by Bauer[10] in 1906, the prothrombin time test, with the bedside technic of Smith and associates,[5] and the serum phosphatase test.[11] The hippuric acid excretion test, as clinically employed by Delprat and Whipple,[12] did not give accurate results in normal dogs with sufficient consistency to warrant its use in the experimental data. Also, the important cephalin-cholesterol flocculation test, described by Hanger,[13] could not be used for the reason that the serum of normal dogs is flocculated by this technic. Control tests were performed on normal dogs.



Mean blood pressure readings for experimental animals.

RESULTS

The normal values used for the various tests may be listed as follows: Values of 1 to 4 mg. of serum phosphatase per hundred cubic centimeters of serum were considered normal. The mean prothrombin time calculated for normal animals averaged eleven seconds. Any excretion of more than 1.5 Gm.

6. Price, P. B.; Hanlon, C. R.; Longmire, W. P., and Metcalf, W.: Bull. Johns Hopkins Hosp. **69**:327 (Oct.) 1941.

7. Moon, V. H.; Morgan, D. R.; Lieber, M. M., and McGrew, D.: Similarities and Distinctions Between Shock and Effects of Hemorrhage, J. A. M. A. **117**:2024 (Dec. 13) 1941.

8. Harkins, H. N.: Surgery **9**:231 (Feb.) 1941.

9. Rosenthal, S. M., and White, E. C.: Clinical Application of Bromsulphalein Test for Hepatic Function, J. A. M. A. **84**:1112 (April 11) 1925.

10. Bauer, A.: Wien. med. Wchnschr. **56**:20, 1906.

11. Gutman, A. B.; Olson, K. B.; Gutman, E. B., and Flood, C. A.: J. Clin. Investigation **19**:129 (Jan.) 1940.

12. Delprat, G. D., and Whipple, G. H.: J. Biol. Chem. **49**:229 (Nov.) 1921.

13. Hanger, F. M.: J. Clin. Investigation **18**:261 (May) 1939.

of galactose was regarded as indicative of impaired hepatic function. The control animals which were submitted to the galactose tolerance test never excreted more than 1 Gm. of galactose. Twenty grams, or half of the standard clinical dose, was used. All the animals in the series approximated 15 Kg. in weight; so the dose was not varied. Retention of 35 per cent or less of sulfobromophthalein sodium in five minutes and of a trace or less in thirty minutes was regarded as normal.

The result of the prothrombin time test was 100 per cent of normal for 4 animals, 92 per cent of normal for 2, 84 per cent of normal for 4 and 73 per cent of normal for 1 animal, the last result indicating perhaps slight impairment of hepatic function. The results for the control animals were 100 per cent of normal except for 1, which was 92 per cent of normal.

The serum phosphatase values were within normal limits for all animals.

hemorrhage, was to estimate the effect of massive experimental hemorrhage on the functions of the liver.

The sulfobromophthalein sodium test gave entirely normal results for 8 of 11 dogs, and results for the other 3 animals were just barely above the upper limits of normal.

The serum phosphatase readings were within the range of normal variation. Drill, Annegers and Ivy,[14] in recent experimental work, concluded that the serum phosphatase level is of definite value in determining impairment of hepatic function.

The prothrombin time was normal or within the variations of normal for 6 of 11 animals. However, for 1 animal a result of 73 per cent of normal was still 33 per cent above the prothrombin time at which a tendency to bleeding is supposed to occur.

The galactose tolerance test was the only one that consistently showed results indicative of

Results of Tests of Hepatic Function

Number of dog	1	2	3	4	5	6	7	8	9	10	11
Retention of sulfobromophthalein sodium											
5 minutes	45%	30%	30%	25%	50%	40%	30%	5%	20%	35%	Trace
30 minutes	5%	Trace	0	0	15%	10%	5%	0	0	Trace	0
Prothrombin time, per cent of normal	92	84	100	84	84	73	100	92	100	100	84
Galactose tolerance, Gm.	0.937	1.5	1.66	3.69	2.59	0.651	8.73	4.04	4.59	3.19	4.94
Serum phosphatase, mg./100 cc.	1.12	1.80	1.19	1.91	1.66	2.05	1.27	1.25	1.69	1.44	2.11

The sulfobromophthalein test gave results within normal limits for all but 3 animals, which had a retention of the dye slightly above the normal limit.

The galactose tolerance test revealed an excretion above normal in 8 of the 11 animals, indicating hepatic impairment in those animals. Those animals were not checked to see if the galactose tolerance returned to normal later.

COMMENT

Shock as mentioned in this paper refers only to the syndrome of shock produced by hemorrhage and accompanied by peripheral circulatory failure with vasoconstriction, hemodilution and a rapid, easily compressible pulse. Blalock stated: "The blood loss that will produce death in dogs is approximately five per cent of the body weight." The amount of blood withdrawn from our animals was slightly less; however, we endeavored to produce only sublethal hemorrhage, and the bleeding time was limited to thirty minutes.

The purpose of these experiments, avoiding entirely the controversial subject of shock versus hepatic damage, the excretion of galactose being above normal for 8 of 11 animals. Any excretion of galactose above 1.5 Gm. was considered abnormal or denoting a damaged hepatic parenchyma. Of the 8 animals with excretions above normal, 6 excreted 3.69 Gm. or more. Seven animals excreted 2.59 Gm. or more, and 1 animal excreted 8.73 Gm., or over a third of the initial dose of 20 Gm.

In summarizing the experimental work of the various workers for the past few years, we noted a general agreement that the galactose tolerance test is one of the most valuable of the various tests of hepatic function, in contradistinction to the opinion of DeLor and Reinhart, who concluded that the galactose tolerance test was the least reliable one used in their series. However, most workers are in agreement that its greatest value lies not in its ability to detect the amount of hepatic damage but in its aptitude to differentiate, in a large percentage of cases, icterus due to mechanical block from that of the toxic or infectious type.

14. Drill, V. A.; Annegers, J. H., and Ivy, A. C.: Proc. Soc. Exper. Biol. & Med. **54**:242 (Nov.) 1943.

In an effort to produce even a finer dividing line between sublethal hemorrhage produced on the initial attempt and death small amounts of blood were removed daily, postoperatively, in an endeavor to reach a level which would still be compatible with life. However, this additional bleeding was not successful because we had no means by which to gage how the amount of blood removed would be tolerated. The removal of only small amounts, of from 10 to 30 cc., invariably resulted in death almost immediately. This agrees with the work of Price and co-workers, who stated that in the late stages of posthemorrhagic shock dogs become extremely sensitive to loss of blood, so that even the loss of only a few cubic centimeters may precipitate collapse of the circulation. Obviously, if enough animals were bled sooner or later an occasional dog would be bound to survive long enough to have tests of hepatic function performed at a time when the parenchymatous organs had been affected by the general anoxia due to massive experimental hemorrhage.

Although the irreversible changes due to anoxia in the parenchymatous organs occur after hemorrhage, they appear only after anoxia has been present for a sufficient length of time. Seven of the 11 animals in this series which received no supportive therapy still appeared to be in hemorrhagic shock the next day, as evidence by their listlessness and unresponsiveness. This continued evidence of shock with its accompanying anoxia would tend to indicate an anoxia of sufficient duration to produce damage to the parenchymatous organs. However, the fact that in a few days the dogs were up and about and appeared fairly normal on clinical observation seems to emphasize the enormous reserve of the dog's hepatic function, besides the remarkable capability of the animal to recover after hemorrhage. Obviously, from the multiplicity of functions possessed by the liver, no single test will detect impairment of all the functions unless the damage is severe. However, it is generally agreed that if one or two tests give positive results at least a certain amount of hepatic insufficiency exists. In other words, the tests are so insensitive that a positive result must be considered distinctly significant. True, certain tests yield false positive results. The cephalin-cholesterol flocculation test is an example of this, but it was not used in these experiments. The wide margin of safety possessed by the liver, only 30 to 40 per cent being necessary to maintain life (with undoubtedly less in animals), offers a possible explanation of only mild impairment of function produced by hemorrhage in our experiments. Routine determinations of sulfobromophthalein and prothrombin levels for patients after massive operative hemorrhage might aid in solving this question, for patients in posthemorrhagic shock clinically present a picture similar to that described as associated with "liver death."

SUMMARY

Massive acute experimental hemorrhage was produced in 12 dogs.

The sulfobromophthalein sodium, galactose tolerance, serum phosphatase and prothrombin time tests of hepatic function were performed on these animals at varying intervals after the bleeding. Control tests had previously been made on normal animals.

The galactose tolerance test revealed marked impairment of the liver's ability to assimilate galactose, as 8 of 11 animals excreted amounts far in excess of those of the control animals, which were considered normal.

The prothrombin time was prolonged definitely for 4 of the 11 animals.

Results of sulfobromophthalein and the serum phosphatase test were normal.

We believe that definite although slight impairment of hepatic function as evidenced by the results of the tests used in our experiments was produced by massive acute hemorrhage.

ASEPTIC NECROSIS OF THE HEAD OF THE FEMUR FOLLOWING TRAUMATIC DISLOCATION OF THE HIP

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The purpose of this report is twofold: first, to call attention to the possibility of traumatic dislocation of the hip occurring without rupture of the ligamentum teres; second, to record a typical case of aseptic necrosis and deformity of the head of the femur with its ligamentum teres intact and thoroughly vascularized, the pathologic condition having arisen from a traumatic interruption of the blood supply of the femoral head coming through the capsule of the hip joint.

It had been my impression [1] that aseptic necrosis of the femoral head following a traumatic dislocation of the hip was the result of two factors: (1) rupture of the ligamentum teres during the dislocation, with consequent deprivation of its blood supply to part of the femoral head, especially to the summit of the head, and (2) too early weight bearing, with collapse of the osseous lamellas before adequate regeneration of bone. My belief was seemingly confirmed by the conclusions of Banks and Phemister.[2] The clinicopathologic picture seemed dependent on a rupture of the capsule of the hip joint and more particularly on a rupture of the ligamentum teres, a tear of which was apparently inevitable in a traumatic dorsal dislocation. Early roentgen examination showed involvement mainly of the top, or proximal, portion of the femoral head, explicable on the basis that the blood supply was cut off from the ligamentum teres and an anemic infarct was formed. Later changes, or irregularities of the femoral head, islands of necrotic bone and marginal osteophytes were the result of aseptic necrosis of the bone and nature's efforts at repair.

Aseptic necrosis encountered in other conditions, such as Legg-Perthes disease, had been assumed to be a direct result of interference with the blood supply coming to the femoral head through the ligamentum teres. This assumption was based mainly on experimental work,[3] in which section of this ligament led to gross and histologic changes in the femoral head which were identical with those observed in Legg-Perthes disease. Several years ago, in studying the ligamentum teres removed at operation in cases of Legg-Perthes disease and cases of slipped femoral epiphysis, I [4] was surprised to find that in at least several cases of Legg-Perthes disease the ligamentum teres had patent and adequate arteries and veins which showed no disease of their walls and were apparently normal. It then became apparent that aseptic necrosis of the femoral head was not always a sequel to an interruption of the blood supply from the ligamentum teres.

The case to be reported is another interesting instance of aseptic necrosis of the femoral head following a traumatic dislocation in which exposure of the hip some time after the injury showed a normal ligamentum teres with patent blood vessels and no scars to indicate a previous injury. The pathologic condition must have resulted from damage to the capsular vessels. This experience refutes my own impression and the opinion of others [2] that the ligamentum teres is ruptured in every case of traumatic dorsal dislocation of the hip.

It is now common knowledge from numerous angiologic studies that the femoral head has three sources of blood supply, namely, the ligamentum teres, the capsular vessels and the vessels in the femoral neck. The amount of blood from each of these sources varies at different ages and in

Read before the Orthopaedic Section of the New York Academy of Medicine on April 21, 1944.

1. Kleinberg, S.: Aseptic Necrosis of the Femoral Head Following Traumatic Dislocation, Arch. Surg. **39**: 637 (Oct.) 1939.

2. Banks, S. W.: Aseptic Necrosis of Femoral Head Following Traumatic Dislocation of the Hip, J. Bone & Joint Surg. **23**:753 (Oct.) 1941. Phemister, D. B.: Fractures of Neck of Femur, Dislocation of Hip, and Obscure Vascular Disturbances Producing Aseptic Necrosis of Head of Femur, Surg., Gynec. & Obst. **59**: 415 (Sept.) 1934.

3. Zemansky, A. P., Jr., and Lippman, R. K.: The Importance of the Vessels in the Round Ligament to the Head of the Femur During the Period of Growth, and Their Possible Relationship to Perthes' Disease, Surg., Gynec. & Obst. **48**:461 (April) 1929.

4. Kleinberg, S., and Friedman, E.: Observations on the Vascularity of the Ligamentum Teres, Bull. Hosp. Joint Dis. **1**:72 (July) 1940.

different persons. Generally speaking the supply through the ligamentum teres is less than through the other avenues. One is reminded of the work of Wolcott,[5] who in recent years and with wider experience concluded that the blood supply entering the ligamentum teres was of minor importance in contrast to the rich supply from the capsule and the periosteum.

REPORT OF A CASE

A. H., a man 20 years of age, was admitted to my service on Dec. 9, 1941, because of pain and stiffness in the right hip and a limp. Four years previously he was injured in a ball game, sustaining a dislocation of the right hip. He was taken to a hospital, where the dislocation was promptly reduced. A splint was not applied, and after rest in bed for two weeks he

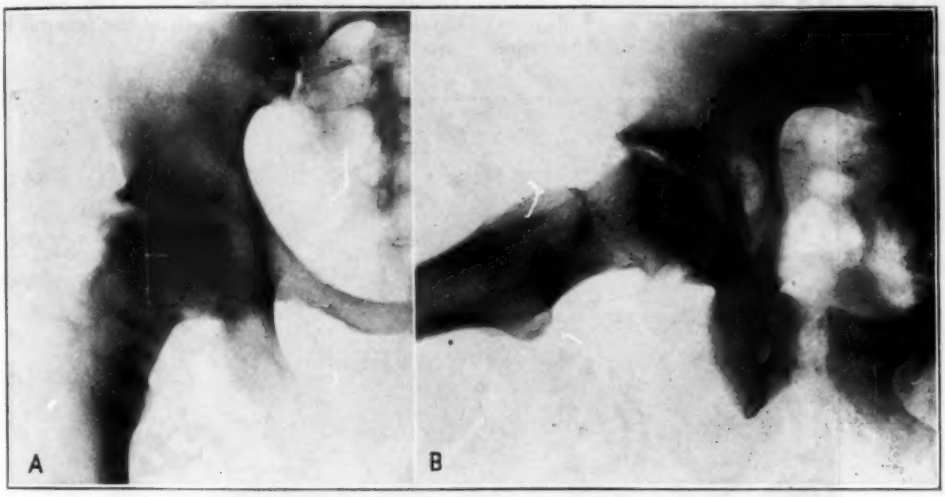

Fig. 1.—*A*, anteroposterior roentgenogram of the right hip, showing marked enlargement and irregularity of the femoral head, considerable reduction in the vertical diameter of the head and numerous vacuolated, or porotic, areas and patches of sclerosis. There is some formation of new bone at both the superior and the inferior border of the head. The epiphysial line has disappeared. *B*, lateral roentgenogram of the hip, showing flattening and irregularity of the articular surface of the head, several clearly visualized vacuolated areas and extensive sclerosis. There is periosteal formation of new bone on the inferior border.

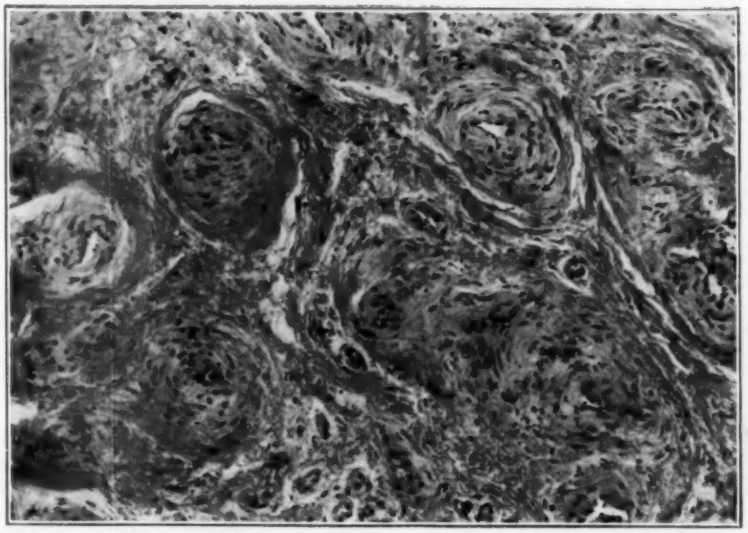

Fig. 2.—Section of the ligamentum teres (× 100). There are numerous patent blood vessels and no evidence of a tear or reparation in the connective tissue to indicate an injury. The walls of the arteries are thickened but not to an abnormal degree.

5. Wolcott, W. E.: Circulation of the Head and Neck of the Femur: Its Relation to Nonunion in Fractures of the Femoral Neck, J. A. M. A. **100**:27 (Jan. 7) 1933.

was allowed to walk. One year later he began to have occasional slight pain in the hip. The pain gradually became more frequent and more severe. During the year before I saw him his physical activity had been hampered and increasingly restricted, so that just prior to his admission to my service he was able to walk only about four blocks without great discomfort.

Physical examination showed that the patient walked with a limp on the right side. The motions in the hip were restricted. Extension was possible to 180 degrees, but flexion was checked at 70 degrees. Inward rotation was limited to a few degrees only and outward rotation to about 30 degrees. Adduction was free, but abduction was checked at 5 degrees. There was no shortening of the right limb, but there was an atrophy of the thigh of 1¾ inches (4.5 cm.) and of the leg of about ½ inch (1.3 cm.).

Roentgenograms showed an extensive change in the shape and structure of the femoral head (fig. 1). The head was enlarged and irregular; its outer surface extended somewhat beyond the acetabulum. Within the head were numerous porotic, or vacuolated, areas (seen especially in figure 1 *B*) and spotty sclerotic patches. The upper surface of the head was depressed, and the articular surface was irregular. There was a periosteal thickening on the inferior border of the neck. The lateral view showed great distortion of the head with partial absorption of the outer part of the head and numerous areas of rarefaction and sclerosis. The epiphysial line had disappeared. The roentgenologist's diagnosis was aseptic necrosis of the femoral head, with which I concurred.

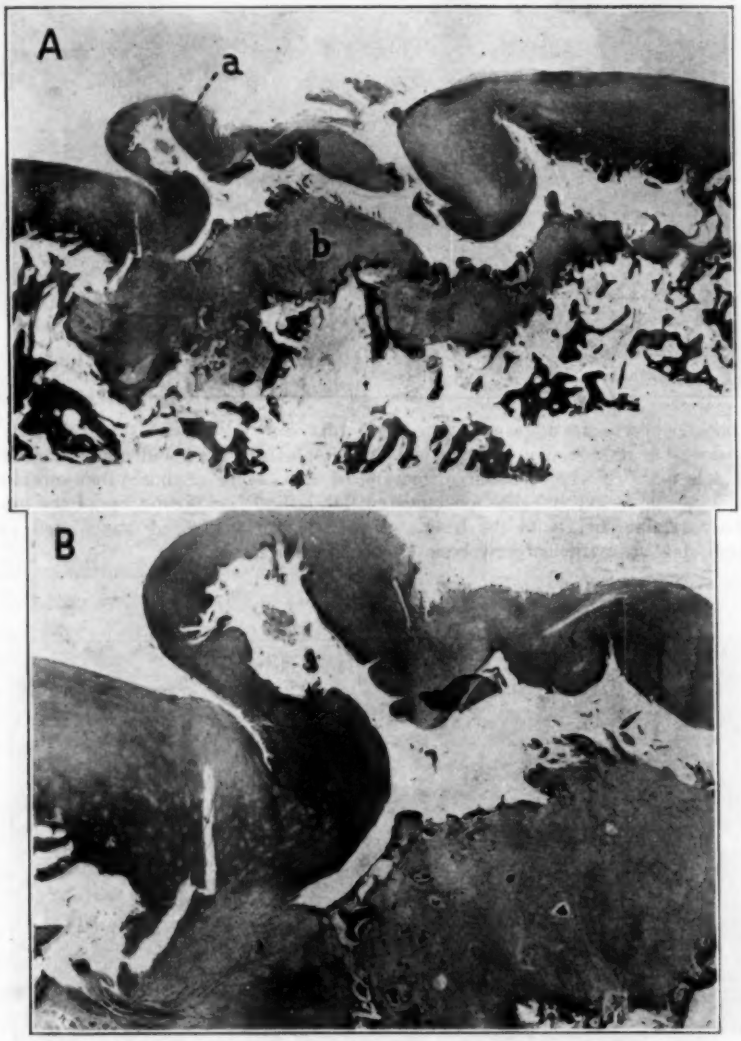

Fig. 3.—*A*, section of articular cartilage and bone (× 5). Note folded, partly necrotic articular cartilage at *a*. At *b* there is hyalinized connective tissue containing subchondrally bits of osseous detritus. *B*, same section as in figure 3 *A* (× 20). This shows the folded partly necrotic cartilage with subchondral bits of dead bone.

The patient evidently had osteoarthritis of the right hip secondary to aseptic necrosis of the femoral head which followed a traumatic dislocation of the hip. An arthrotomy of the hip joint for the purpose of doing an arthroplasty gave me an opportunity to inspect the whole hip joint. The capsule of the hip joint appeared normal in thickness and color and, grossly at least, exhibited no recognizable signs of previous injury. The ligamentum teres was attached to the top of the femoral head at what seemed logically the fovea.

Sections of the capsule, the ligamentum teres, the articular cartilage and the femoral head were removed for microscopic study. Pathologic examination showed that the synovial lining of the capsule was thickened. The articular cartilage was indented in many areas. In all of the osteochondral fragments removed from the head there were subchondral cystic fibrous nodules, some as large as 1 cm. in diameter; these corresponded to the rarefied areas in the roentgenograms. The ligamentum teres was well vascularized. Tissues from the femoral head showed a good deal of residual aseptic necrosis, especially subchondrally. Much of the folded cartilage, which was articular cartilage that had folded after the collapse of the subchondral bone, was necrotic, and beneath it there was a layer of fibrous tissue and fibrocartilage.

Thus there were evidences of typical, advanced and extensive aseptic necrosis in the femoral head. The ligamentum teres was normal both grossly and microscopically. An additional interesting feature, noted during the exploration of the hip, was that alterations in the articular cartilage were least marked at the attachment of the ligamentum teres.

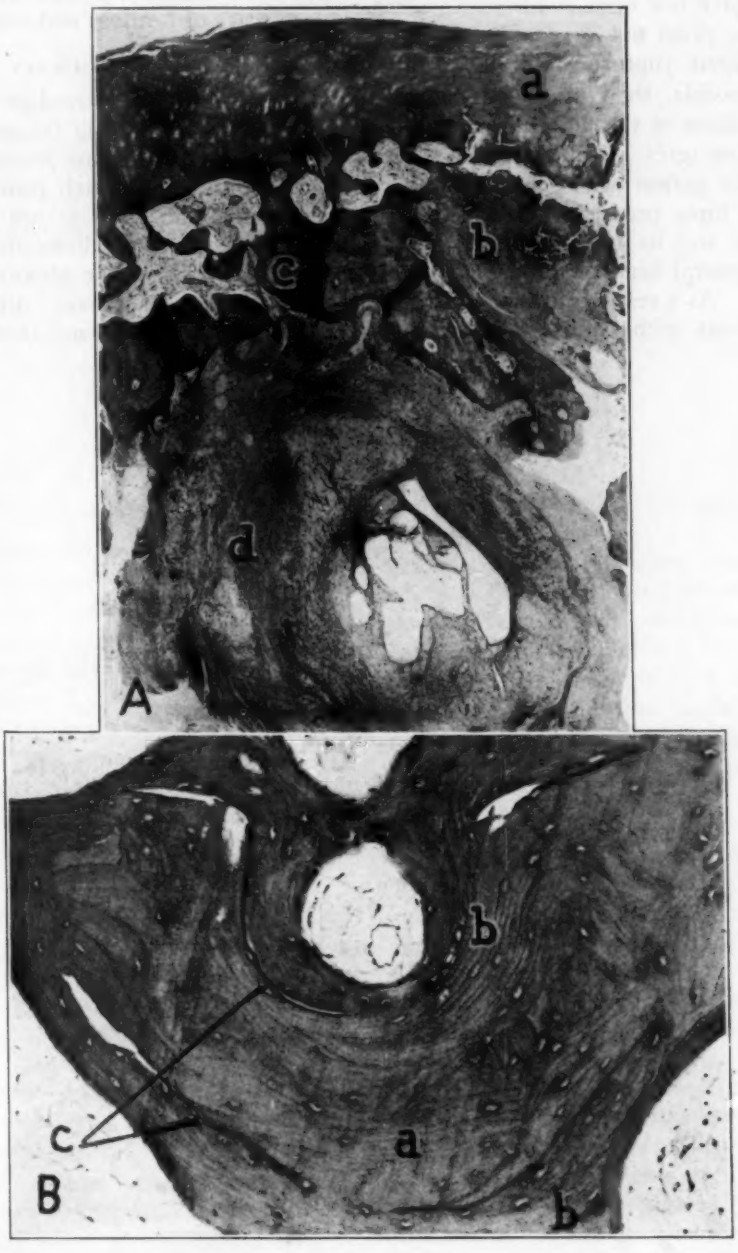

Fig. 4.—*A*, section of articular cartilage and subchondral tissue (× 25): *a*, articular cartilage; *b*, focus of hyalinized connective tissue containing islands of necrotic bone; *c*, modified subchondral bone, some of which has undergone aseptic necrosis; *d*, large focus of cystic fibrous tissue. *B*, subchondral bone (× 150): *a*, dead bone; *b*, living bone; *c*, cement lines.

COMMENT

From experience in operations on the hip joint in which the femoral head is deliberately dislocated from the acetabulum, I have learned that, whereas most of the time the ligament is torn, not at all infrequently, particularly if manipulations have not been sudden or violent, the head can be pried out or eased out of the acetabulum without rupturing the ligamentum teres. It is possible, therefore, to visualize a traumatic dislocation of the hip without rupture of the ligamentum teres. That must have been the case with the patient whose history is here recorded. The force producing the dislocation tore the capsule and its blood vessels, thereby depriving the femoral head of a large source of its blood supply. As a result of this there ensued an aseptic necrosis with collapse of the bony structure, arising from too early weight bearing. One might, of course, postulate that the ligamentum teres had been torn but that the fragments had fortuitously come accurately and intimately in contact after the reduction and had reunited. But in such an event, which is extremely unlikely, there would remain at least some scars of healing, and none were visible.

SUMMARY

In an instance of proved aseptic necrosis of the femoral head following traumatic dislocation of the hip, the important finding was a normal ligamentum teres, which proves that rupture of the ligamentum teres is not a constant occurrence in a traumatic dislocation and that typical aseptic necrosis of the femoral head may occur even though its blood supply through the ligamentum teres has not been disturbed.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from page 74)

BLADDER

Tumor.—Rathbun and Wehrbein [28] state that lymphosarcomatous tumor of the urinary bladder is rare; data on only 5 cases have been reported previously. The case they reported was of a woman, 64 years of age, who gave a history of recurrent cystitis. Cystoscopy revealed two round tumors in the right side of the base of the bladder and two small ones on the left lateral wall. The bladder was opened, and the tumors were excised with fulgurating current. The histologic diagnosis was lymphosarcoma of the bladder.

Hourglass Deformity.—Zellermayer and Carlson [29] state that true congenital hourglass bladder is a definite entity and is caused by some regular malformation in the development of the embryo. The bladder is divided into two portions, one above the other, so that it has the shape of an hourglass. In some instances the ureters open into the upper segment and in other instances into the lower segment.

Three hypotheses have been advanced to explain the formation of congenital hourglass bladder, all of which seem plausible—atavistic relationship to hourglass bladder normally found in some animals, persistence of the embryonic ureteric membrane and unequal growth of the two vesical anlages.

Usually it is the symptoms of cystitis that bring the patient to the physician. Many patients give a history of lifelong vesical disturbance. These symptoms include difficulty of urination, dysuria or history of enuresis.

Congenital hourglass bladder can be recognized readily by cystoscopic examination. When the cystoscope is introduced into the bladder it is seen that the bladder is divided into two compartments, one above the other. The opening between the two segments may vary from 1 cm. to 5 or 6 cm. in diameter. The upper segment is seen to contain normal trabeculations and vascular markings, while the walls of the lower segment are smooth. The capacity of the hourglass bladder without secondary inflammation is that of the normal bladder. When acute cystitis is present, the capacity is limited. The constricting band separating the two segments is thick and does not present a sharp edge, seen in cases in which there is a diverticulum. The band also is seen to extend around the anterior vesical wall and does not blend into the lateral walls of the bladder. The ureters may open into the upper segment.

The treatment of congenital hourglass bladder should be directed toward the enlargement of the opening between the two halves of the hourglass, so as to allow better drainage and more complete emptying of the bladder. In 11 of 22 cases collected from the literature, some opera-

28. Rathbun, N. P., and Wehrbein, H. L.: Lymphosarcoma of the Urinary Bladder, J. Urol. **51**:31-36 (Jan.) 1944.

29. Zellermayer, J., and Carlson, H. E.: Congenital Hourglass Bladder, J. Urol. **51**:24-30 (Jan.) 1944.

tive procedure directed at the removal of the fibrous ring was done. Of the 11 patients on whom operation was performed, 9 recovered. In 5 cases the ring was cut with scissors through a suprapubic incision; in 2 cases the base of the bladder was resected, and in 2 cases the entire muscular band was excised: In 1 case it was cut through a perineal incision, and in 1 case its was divided transurethrally.

The patient with hourglass bladder reported on by Zellermayer and Carlson was a man aged 38 who complained of frequency of urination, fifteen to twenty times daily, with occasional burning on urination and nocturia (ten to fifteen times). Cystoscopic examination did not show any urethral obstruction. When the cystoscope was introduced into the bladder, it was seen that the bladder was divided into two separate segments, which were about equal in size. They were both much inflamed. However, it could be seen that the surface of the lower segment was evidently smoother than that of the upper segment. The capacity of the entire bladder was 100 cc. The dividing ridge was seen to encircle the bladder completely and was more prominent posteriorly than anteriorly. The opening between the two compartments was estimated to be about 3 cm. in diameter. Search for the ureteral orifices showed that they were practically on the ridge separating the two halves of the bladder. The lower portion of the bladder blended with the posterior urethra, so that no real narrowing was seen until the verumontanum was encountered. In the posterior urethra there were openings to fifteen or twenty sinuses, none of which was more than 1 cm. in depth. Digital examination showed that the prostate was normal in size and contour. Pus could not be forced from these sinuses by the examining finger. A cystogram was made, 100 cc. of skiodan solution being used. The cystogram showed the typical hourglass deformity. After the patient had taken sulfathiazole, the urine became clear and free of pus. Since the patient was so much improved, he decided to defer surgical treatment temporarily.

Rupture.—Moroney [30] reports a case of spontaneous rupture of a tuberculous bladder. The patient, a woman aged 22 years, complained of pain in the lower part of the abdomen and anuria of twenty-eight hours' duration. She had had frequency of micturation for two years. Her father had died from phthisis. On examination, there was generalized tenderness over the lower part of the abdomen. Urine was not obtained from the bladder by catheterization. The abdominal cavity was explored and found to contain urine. On the posterior wall of the bladder there was a small perforation from which urine was exuding. The pelvis was drained, and an extraperitoneal suprapubic fistula was established. The patient died a week later. Tubercle bacilli were recovered from the urine. At necropsy a diagnosis was made of bilateral renal tuberculosis with extension to the ureters and to the bladder.

Bilharziasis.—Newman [31] states that bilharziasis of the bladder is rare in England and that Schistosoma haematobium is the most common causative agent. The pathologic lesion consists of a diffuse infiltration of the submucous layer or the formation of papillomas. The papillomas usually are situated in the regions of the ureteral orifices. The earliest symptom is commonly intermittent, painless hematuria, severe urinary frequency being an extremely late symptom. Intravenous administration of sodium antimony tartrate, together with endoscopic resection of papillomas in selected cases, is the treatment of choice.

Incrusted Cystitis.—Herger, Sauer and Neter [32] employed "solution G," a solution of citric acid, magnesium oxide and sodium carbonate of p_H 4, in the treatment of 21 patients who had persistently alkaline urine with a tendency to formation of stones and incrustations.

The solution was administered as a rule by continuous drip irrigation through a three way Foley bag catheter for one to four weeks. Treatment was well tolerated by all but 1 patient, who had an incrusted carcinoma in the region of the vesical sphincter.

The most favorable results were obtained in 13 cases of incrusted vesical ulcerations. Cure with formation of a scar took place in 8 of these cases; in 4 the patients showed decided improvement, and in 1 the patient responded with temporary improvement after treatment for only one week.

Incrustations disappeared in 4 or 5 cases of incrusted carcinoma of the bladder.

In 1 of 2 cases of urinary calculi treatment resulted in dissolution of one of two stones in the renal pelvis, and in the other case, in regression of the size of the calculus.

30. Moroney, J.: A Case of Spontaneous Rupture of a Tuberculous Bladder, Brit. J. Surg. **31**:98 (July) 1943.

31. Newman, H. R.: Transurethral Surgery in Relation to Bilharziasis of the Bladder, J. Urol. **50**:440-445 (Oct.) 1943.

32. Herger, C. C.; Sauer, H. R., and Neter, E.: The Value of the Stone Dissolving Agent, Solution G, in the Treatment of Alkaline Incrustations of Bladder Lesions, Surg., Gynec. & Obst. **77**:634-638 (Dec.) 1943.

In addition, acidification of the urine was accomplished in 1 case in which suprapubic cystostomy had been performed for carcinoma of the prostate.

Complete bacteriologic studies were carried out in 9 of the 21 cases. Although sterilization of the urine was not achieved in any of these 9 cases, it was found that treatment resulted in marked reduction of the number of organisms in 5 cases.

PROSTATE GLAND

Cancer.—Nesbit and Cummings [33] conducted a second follow-up study on a series of patients treated by orchiectomy for prostatic cancer. The study gave continued evidence of the value of this form of treatment.

Forty-five per cent of the patients remained free from symptoms twenty-one to thirty-six months after orchiectomy, but 21 patients previously reported as showing favorable response have had recurrent symptoms of advanced disease, and several of these have died. The increasing incidence of delayed failure in this series suggests that eventually all patients may fall into this category.

It is evident that endocrine therapy increases the life expectancy of patients who have prostatic cancer by causing a suppression of carcinogenic activity for temporary but varying periods and that this temporary control is accompanied clinically by a period of relief from symptoms resulting from the malignant disease. Maximal benefit to the patient may be derived by delaying endocrine treatment until it is indicated by the onset of symptoms arising from advanced or metastatic lesions. Only in this manner can the longest period of palliative relief be assured.

Huggins [34] emphasizes that the results of orchiectomy in the treatment of prostatic cancer are not uniformly successful and that they fall into three groups: In one group, the patients (less than 5 per cent) received no or slight benefit from endocrine treatment; in the other groups, which were larger and contained a nearly equal number of patients, an improvement pronounced but unsustained (less than eighteen months) and a pronounced and more prolonged regression of the disease were obtained respectively. The improvement is greater than the palliation, which implies technically that the patient is merely made more comfortable in the face of advancing disease. The benefit in cases of prostatic cancer often includes disappearance of the tumor, at least grossly, and is considered as inhibition of the neoplasm. In clinical cases castration seems to give somewhat better results than occur from estrogenic therapy. Huggins adds that if nothing more were accomplished from the endocrine treatment of advanced prostatic cancer than a decrease of hours of pain, which often occur, the results would be clinically desirable at the present. Often greater benefits occur.

Huggins,[35] in summarizing his work on effects of endocrine treatment in cases of advanced prostatic cancer, emphasizes two points: first, that cancer of the prostate gland is often extremely sensitive to androgens; second, that the study of any disease, and especially cancer, is expedited greatly by development of objective laboratory methods of following its course.

In a series of 47 men who had advanced prostatic cancer, it was found that 24 had elevation of the amounts of acid and alkaline phosphatase, while the enzymes of the other 23 men were in the normal ranges. By frequent observation of the serum phosphatase values of men who had far advanced prostatic cancer with elevation of the serum phosphatase, it was found that decreasing the amount or the activity of the androgens by castration or by administration of estrogen (diethylstilbestrol, 1 mg. daily) caused a decrease of serum acid phosphatase values, whereas administration of androgen (testosterone propionate, 25 mg. daily) caused an increase of the serum phosphatase values and an exacerbation of the disease.

Certain benefits usually follow orchiectomy. Among the earliest changes are increased appetite and relief of pain. These effects often are observed within several days after castration. They result in a gain of weight and an improvement of the anemia. Frequently there is a recession of the primary tumor, so that the hard, nodular, craggy prostate gland becomes smooth and soft and decreases greatly in size. Changes often are observed in the metastatic growths in the bones on roentgenographic examination, the metastatic lesions usually undergoing increased calcification within several months after orchiectomy. This increased density is often followed by stabilization of growth or by disappearance of the metastatic growths to roentgenographic examination.

In the entire series of 45 men on whom orchiectomy was performed, there have been 8 deaths,

33. Nesbit, R. M., and Cummings, R. H.: Prostatic Carcinoma Treated by Orchiectomy: A Secondary Report Based on Seventy-Five Cases Observed for at Least Twenty-One Months Following Operation, J. A. M. A. **124**:80-81 (Jan. 8) 1944.

34. Huggins, C.: Orchiectomy in the Treatment of Prostatic Cancer, J. A. M. A. **124**:122 (Jan. 8) 1944.

35. Huggins, C.: A Summary of Endocrine Effects in Advanced Prostatic Cancer, New York State J. Med. **43**:519-521 (March 15) 1943.

all of men who had extensive metastatic growths to bone. In 4 of these men carcinomatosis was the principal cause of death, while in the others it was of secondary importance. From a clinical standpoint, 31 men have had sustained improvement lasting as long as thirty months; 9 men have had temporary improvement followed by recurrence of symptoms and 5 men did not improve after castration.

In 11 of the group of 21 men on whom operation was performed twelve to thirty months prior to the report, there had been significant improvement. Roentgenograms revealed that in 4 men extensive osseous metastatic growths had disappeared completely.

Inactivation of androgens by estrogens is unsound, since the inhibition of the androgens is not complete, and a complete inhibition or elimination of androgens is the basis for the modern treatment of advanced prostatic cancer. Moreover, this partial inhibition is temporary and estrogen must be administered for long periods. Furthermore, in many species the administration of estrogen to men for an extended length of time has in itself a carcinogenic effect.

Kahle, Schenken and Burns [36] discuss 7 cases of adenocarcinoma of the prostate gland (diagnosis in six proved by biopsy) in which treatment with diethylstilbestrol or diethylstilbestrol dipropionate has been given since March 1940. Detailed data on these cases were reported in February 1942, and the data on 5 cases which could be followed are brought up to date in this communication. In 4 cases improvement of general health and of local conditions and relief of symptoms previously reported had continued to the time of the report. The fifth patient died of urinary sepsis and cardiac failure.

In all 5 cases, including that in which the patient died, serial histologic examination showed definite regression of the carcinomatous tissues. There were a regression of metastatic osseous lesions, as demonstrated by serial roentgenologic examination, in the single case in which such lesions were present and a regression of metastatic lesions to the lymph nodes in another instance.

Massive doses of diethylstilbestrol and of diethylstilbestrol dipropionate were used without ill effects except for transient gynecomastia in a single instance. In 1 case in which there was an apparent recurrence of the carcinomatous process a second course of treatment was as effective as the first in controlling symptoms and causing a demonstrable regression of the malignant neoplasm.

The regressive histologic changes observed in diethylstilbestrol-treated carcinomas of the prostate gland, as compared with the histologic changes in untreated carcinomas, may be outlined as follows: 1. In the untreated specimen the neoplastic cells present large vesicular nuclei, prominent nucleoli and granular, reticular cytoplasm. 2. In the first stage of regression there is a decrease of the size of the nuclei associated with condensation of the nuclear chromatin. Nucleoli are no longer visible, and mitoses are absent. Cytoplasmic vacuoles appear and are located predominantly at the bases of the cells. 3. In the second stage of regression the nuclei are pyknotic. The cytoplasm is practically clear, and the cell membranes have ruptured, with resulting coalescence of vacuoles. With the rupture of all the cell membranes, the pyknotic nuclei and the fragments of the membranes are clustered in the centers of the acinar spaces. 4. In the next stage of regression clear acinar spaces contain only remnants of pyknotic nuclei. 5. In the final stage, as Kahle and his associates have observed it so far, only stroma, consisting of smooth muscle and fibrous tissue, remains. Accumulations of lymphocytes and macrophages and deposits of brown pigment are present in some parts of the stroma.

Kretschmer [37] believes that not enough time has elapsed since the procedure of orchiectomy was instituted to talk about cures in cases of carcinoma of the prostate. The conclusions are hasty, since most statistical studies on the curability of cancer are based on five and ten year cures. He states that his results have not been as satisfactory as one would be inclined to believe they should be, judging from the literature. He reports his experience with 11 cases. Three of the patients were dead five, eight and eleven months respectively after orchiectomy; 1 patient was bedridden, requiring frequent doses of morphine; 3 patients had pain; 1 patient had painful urination and attacks of hematuria; 1 patient stated that his condition was improved eleven months after orchiectomy, another seven and a half months after and 1 four months after. Some of the patients experienced a feeling of well-being immediately after orchiectomy. For 2 of the patients who died the feeling of well-being was indeed short. In the evaluation of this form of treatment it should be remembered that for cancer in other parts of the body statis-

36. Kahle, P. J.; Schenken, J. R., and Burns, E. L.: Clinical and Pathologic Effects of Diethylstilbestrol and Diethylstilbestrol Dipropionate on Carcinoma of the Prostate Gland, J. Urol. **50**:711-732 (Dec.) 1943.

37. Kretschmer, H. L.: Orchiectomy in the Treatment of Cancer of the Prostate Gland, J. A. M. A. **123**:755-757 (Nov. 20) 1943.

tical results are based on five or ten year studies of so-called cures.

Sarcoma.—Kirshbaum, Larkin and Culver [38] report a case of reticulum cell (retothel) lymphosarcoma in a man aged 25 years. The patient lived for three years with roentgen treatment. The tumor metastasized locally and to distant organs. Obstruction to the ureteral orifices produced clinically the terminal picture of uremia. There was associated moderate hypertension. Data on 15 cases of lymphosarcoma have been collected from the literature, including those on the case presented here.

Hypertrophy.—Moore [39] presents a morphologic study of benign hypertrophy of the prostate gland, which, he states, occurs with increasing frequency after 40 years of age, but the cases in which there are clinical symptoms of urinary obstruction reach a maximal incidence at 65 years of age. This would indicate that the etiologic agent is most active during presenility.

Observations suggest that married men are affected more frequently than might be expected from the distribution of the general population. The yellow race apparently is less affected with benign hypertrophy than the white or the black race. Members of the white race do not show any variation of incidence in different parts of the world.

The sexual drive of patients who have benign hypertrophy is probably not altered significantly. The first demonstrable lesion in prostatic hypertrophy is hyperplasia of the periductal, periacinar and periurethral stroma. In rare instances hyperplasia of epithelium is primary.

Nodules associated with prostatic hypertrophy are derived most commonly from the stroma and the glands of the part of the prostate gland frequently designated as the inner group of glands. This includes the periurethral glands and the acini anterior and medial to the ducts of the lateral lobes. The true middle lobe of the prostate gland is involved less frequently, the anterior lobe rarely and the posterior lobe very rarely, if at all.

The typical epithelial cell of the hypertrophic prostate resembles that of the adult prostate gland but differs from it in the relative absence of definite secretory activity. The stroma differs from the normal in a relative richness of smooth muscle and absence of elastic tissue. Prostatic hypertrophy is associated with development of masses of lymphoid tissue, an appearance frequently mistaken for an inflammatory infiltration of lymphocytes. Nodules composed only of smooth muscle are not distinctive but represent a variant in which the stromal hyperplasia does not include glands.

There is no histologic basis for the hypothesis that selective arteriosclerosis in the outer group of glands is the cause of prostatic hypertrophy. Inflammation may occur in the prostate gland in association with benign hypertrophy but is not the cause of the disease.

Degenerative changes in the epithelium and the stroma are not of special significance. The uninvolved part of the prostate gland in cases of benign hypertrophy shows atrophy and atypical hyperplasia, the histologic evidence of irregular or abnormal stimulation. Metaplasia of the epithelium of the prostate gland frequently occurs, but the histologic evidence alone is insufficient to postulate powerful estrogenic stimulation as the cause.

Carcinoma in a nodule which has undergone benign hypertrophy without involvement of the surrounding tissue is rare. When a carcinoma is present in both the tissues that have undergone benign hypertrophy and the neighboring prostatic tissue, no conclusions in regard to its origin are possible. Material derived from surgical operation is valueless in this connection, since only part of the prostate gland is available for study.

Recurrence of prostatic hypertrophy may be due to growth of nodules not removed at the first operation or to development of new nodules.

After suprapubic prostatectomy, the compressed posterior and lateral lobes expand by stromal growth to surround the large prostatic urethra.

The enlarged prostate gland of old dogs is not comparable anatomically to the benign hypertrophic prostate gland of man.

Melick [40] reports that in 4 cases in which a one stage suprapubic prostatectomy was done and in 19 cases in which a two stage operation was done a shorter period of healing of the incision was obtained when nylon stay sutures were used than when catgut was used. This suture material has been without any danger to the patients; there have been no deaths among these patients. These results have been achieved, Melick believes, largely through the technical advantages of nylon over catgut, which he has

38. Kirshbaum, J. D.; Larkin, H. S., and Culver, H.: Retothel Sarcoma of the Prostate Gland: Report of a Case, J. Urol. **50**:597-607 (Nov.) 1943.

39. Moore, R. A.: Benign Hypertrophy of the Prostate: A Morphological Study, J. Urol. **50**:680-710 (Dec.) 1943.

40. Melick, W. F.: The Use of Nonabsorbable Stay Sutures as the Primary Means of Closure in Suprapubic Prostatectomy, J. Urol. **50**:449-457 (Oct.) 1943.

enumerated. The total period of hospitalization, especially for the patients on whom one stage prostatectomies were performed, approaches that for perineal and transurethral prostatectomy; thus one of the chief objections to the suprapubic route has been overcome.

Transurethral Resection.—Orr, Kundert and Pyle [41] review the late results that follow transurethral prostatic resection. Questionnaires were sent to 483 private patients. Of these 483, 407 were traced. One hundred and fifteen were found to have died from within a few months to nine years or more after leaving the hospital. Data obtained on 76 were insufficient for tabulation of the results of their surgical treatment. According to the patients' own statements, 160 of the total 252 with whom contact was made stated that they were satisfied with the results of their surgical treatment. Nineteen stated that they were definitely dissatisfied because they had not been entirely relieved of their symptoms. Intelligible replies were received from 252, and of this number 209 presented themselves for examination.

For the 483 patients treated, a total of 576 prostatic resections were found necessary for one cause or another before relief was obtained.

Multiple operations were planned for 31, but because of the unusual size of the gland the number was increased to 39. The remaining 452 patients had only one resection for what was believed at the time to afford satisfactory relief of the obstruction. A second operation, because of insufficient removal or regrowth of tissue, was found necessary for 44 patients, who returned to the hospital after their original operation. Of these 44, 1 patient returned six different times for removal of rapid regrowth of tissue over six years. Two patients were readmitted four times for recurrent growth over seven or eight years, and 4 patients were readmitted three times over five to eight years for removal of additional tissue.

It is interesting to note that 46 of the 483 patients had had previous prostatic operations elsewhere, in intervals from twenty years to a few months. Six patients had undergone suprapubic and 6 perineal prostatectomy. Thirty-one had had transurethral resection performed previously.

The smallest amount of tissue removed to afford relief from obstruction was 1 Gm., and the largest amount removed from any 1 patient totaled 117 Gm. The average weight of prostatic tissue removed from the first 250 patients was 12.4 Gm., and from the last 233 patients the average was 15.6 Gm. Twenty-seven patients underwent removal of vesical calculi by litholapaxy or cystotomy, either at the time of the resection or during their initial stay in the hospital. The average number of years of survival after operation was 3.34.

On examination of one or two sections of tissue, malignant prostatic hypertrophy was diagnosed in 45 cases, and in 6 more the condition was diagnosed as malignant on examination of additional tissue—a total of 51 cases in which malignant prostatic hypertrophy was diagnosed at the time of operation.

Of the patients for whom the diagnosis of benign prostatic hyperplasia was made, 31 returned later with unmistakable evidence of malignant changes, which had been overlooked at the time of the first examination. Of these, 9 had additional tissue removed. Of the patients who had known carcinoma of the prostate at the time of operation, 16 were living at the time of the report and 24 were dead.

Gutierrez [42] points out, on the basis of 3 consecutive cases of failure of transurethral prostatic resection in which operation had been performed elsewhere, that this form of operation is not suited to all cases of prostatic hypertrophy and that it has its limitations as well as its indications. In all 3 cases the hypertrophic tissue had been of considerable size (50 Gm., 80 Gm. and 210 Gm.); the operations had been performed five years, four years and three years previously and had been followed through all the intervening years by persistent symptoms, for which the patients had been receiving endless treatment, without relief. These cases serve to prove the obvious failure here of this type of operative treatment, which has been held out as a panacea for all forms of prostatic obstruction. In all these 3 cases the patients were cured by simple perineal prostatectomy, with completely satisfactory results.

Even though transurethral resection sometimes can be repeated safely in two, three, four, five or even more stages, obviously it cannot be recommended if the patient has an enormous prostate gland, weighing more than 200 Gm. At the time of prostatectomy in 1 case reported by Gutierrez the "tunnel" that had been drilled earlier through a prostate gland hard as a rock presented a striking picture. In view of the fact

41. Orr, L. M.; Kundert, P. R., and Pyle, F. J.: Late Results Following Transurethral Prostatic Resection, New York State J. Med. **43**:521-524 (March 15) 1943.

42. Gutierrez, R.: Failures of Transurethral Prostatic Resections: Their Cure by Perineal Prostatectomy, Urol. Letter Club, Oct. 12, 1943, pp. 74-75.

that patients can be offered a permanent cure by an open operation in the form of conservative total prostatectomy, the folly of undertaking to remove extremely large prostate glands through the urethra becomes doubly clear. Gutierrez concludes that the coming generation of urologists should be trained on a surgical basis to use all of the three methods available for relieving prostatic obstruction: transurethral, suprapubic and perineal prostatectomy, including total enucleation of the adenoma, and subtotal and total radical perineal prostatectomy for the removal of cancer of the prostate gland.

Creevy [43] states that loss of blood constitutes one of the principal hazards of transurethral prostatic resection. When excessive, it prolongs the operation, reduces its accuracy and increases the risk of complications and of death. The preliminary injection into the prostate gland of a mixture of isotonic solution of sodium chloride, pitressin and epinephrine hydrochloride in a series of 32 cases of transurethral resection of 30 Gm. or more of prostatic tissue has apparently reduced the loss of blood by 35 per cent and has been without harmful effects. Care must be exercised lest the patient be returned to his room before the vasoconstricting effect of the drugs has worn off.

Milner [44] states that in his hands transurethral resection is the operation of choice. Good results depend on the ability to recognize prostatic tissue when it is encountered and to resect down to the surgical capsule. Postoperative symptoms of cystitis are almost invariably due to leaving tissue to which the blood supply has been destroyed. In all cases of postoperative incontinence cystoscopy should be performed and any tissue impinging within the external sphincter should be removed. No patient capable of living through his preoperative preparation presents too great a risk for resection to be performed.

On the basis of study of a series of 140 cases Kretschmer and Ockuly [45] discuss loss of blood during transurethal resection. No attempt was made to separate carcinoma from benign hypertrophy or large vascular lateral lobes from middle lobes, bars or commissures.

In the first series of 35 cases the loss of blood per resection averaged 281.8 cc. This was considerably higher than had been expected. In the second group of 35 cases the average loss of blood per resection was reduced to 109.7 cc. In the third and fourth groups of 35 cases each the loss of blood was respectively 62.4 and 64.7 cc. These figures represent only the amount of blood lost during resection in the operating room and do not take into consideration the loss of blood after the patient has been returned to his room. It is true that no matter how carefully the bleeding is controlled at the time of the resection some patients will continue to have some bleeding. In rare instances the bleeding may continue for twenty-four hours. This added loss of blood should only emphasize the need for hemostasis at the time of resection. Fulguration, in the opinion of Kretschmer and Ockuly, is the only correct method available for controlling bleeding at the time of resection.

Drainage is not as free through the hemostatic catheter as it is through the straight catheter. This delayed drainage in the presence of bleeding aids in the formation of clots which require irrigation and removal by hand, thereby affording opportunity for contamination and subsequent infection. Kretschmer and Ockuly believe that in cases in which an indwelling hemostatic bag is used the incidence of postoperative chills and fever is slightly greater than in cases in which a hemostatic bag is not used. After checking their records of patients who have slight incontinence for a few days after resection, invariably they found that it occurred in those cases in which a hemostatic bag had been used.

The morbidity and the mortality rate from transurethral resection of the prostate gland are influenced definitely by the loss of blood at the time of resection.

Calculi.—Young [46] reports a case of ochronosis and alkaptonuria in a man in whose urine homogentisic acid was found. Stones were discovered in the prostate gland by roentgenologic examination and removed by perineal prostatectomy, with excellent result. This is the only case in which an operation has been done.

A study of the literature shows that in only 1 case of ochronosis associated with calculi in the prostate gland was the condition discovered clinically. However, no operation was done. Four other cases from the literature in which calculi were discovered in the prostate at necropsy are described.

Ochronosis is characterized by urine of a deep brown color which becomes black on standing. If homogentisic acid is found in the urine,

43. Creevy, C. D.: The Intraprostatic Injection of Pitressin and Adrenalin in the Control of Bleeding During Transurethral Resection: A Preliminary Report, J. Urol. **50**:593-596 (Nov.) 1943.

44. Milner, W. A.: Transurethral Prostatectomy, New York State J. Med. **43**:517-519 (March 15) 1943

45. Kretschmer, H. L., and Ockuly, E. F.: Determination of Blood Loss During Transurethral Resection, J. Urol. **51**:69-71 (Jan.) 1944.

46. Young, H. H.: Calculi of the Prostate Associated with Ochronosis and Alkaptonuria, J. Urol. **51**: 48-58 (Jan.) 1944.

the diagnosis of alkaptonuria is justified. The presence of the telltale dark brown urine, with small black deposits on standing, should arouse suspicion of homogentisic acid and probably will lead to the diagnosis of alkaptonuria more frequently than is shown by the literature.

Huggins and Bear,[47] in discussing the course of prostatic ducts and the anatomic, chemical and roentgen ray diffraction analysis of prostatic calculi, state that prostatic calculi occur in all parts of the epithelial apparatus of the gland, acini and ducts and also in the stoma when they have sloughed through the epithelium. However, the stones requiring surgical treatment—usually the largest ones—are encountered most commonly in the ducts, which they often obstruct, producing cystic dilatation of the acini upstream. The stone-filled ducts display the prostatic ductal paths, which in man course in crescentic fashion between the lateral lobes and the posterior lamella to empty into the urethra lateral to and in the verumontanum and into the utriculus. The position of true prostatic calculi, therefore, in the cases in which intervention is required is in the mouths of the ducts or deep in the gland. In adenomatous hypertrophy of the prostate gland the calculi cling to the surface of the adenoma or remain in the prostatic bed after enucleation; here, too, they locate in the ducts which drain the adenoma, while the calculi in the center of the adenoma are usually of microscopic proportions.

The chemical composition of prostatic calculi varies over a narrow range. The organic components, about 20 per cent, include protein (8 per cent), cholesterol (3.7 to 10.6 per cent) and citrate (0.17 to 2.9 per cent). The principal inorganic constituent is tertiary calcium phosphate, presumably with an apatite constitution. The concentration of carbonate is somewhat less than that in bone; otherwise chemical and roentgen analyses reveal close similarity of the inorganic constituents of prostatic calculi and the bone salt.

Cristol and Emmett[48] studied the incidence of prostatic calculi associated with prostatic hyperplasia and with carcinoma of the prostate gland. The consideration of this relationship is of practical significance, as it has been thought commonly that the presence of stones ruled out the possibility of a malignant lesion. In other words, it was thought that stones occurred only rarely in cases of prostatic carcinoma. Cristol and Emmett's study was based on 4,136 cases of prostatic hyperplasia and 686 cases of carcinoma of the prostate gland. Prostatic calculi were present in 7 per cent of the cases of hyperplasia and in 6.3 per cent of the cases of carcinoma.

Infection.—Henline[49] states that chronic prostatic infections are of common occurrence and that in by far the greatest percentage of cases the infection is not caused by gonorrhea. Infection of the prostate gland occurs more frequently from a distant focus of infection or from some nonspecific infection in the urinary tract. Lack of sexual hygiene may be a predisposing factor in the development of a prostatic infection.

Urinary and genital symptoms frequently attract attention to the prostate gland as the source of the infection. In many instances chronic prostatitis does not present any local or urinary symptoms and attention is not attracted to the prostate gland. A careful prostatic examination is required to determine that the prostate gland is a focus of infection which causes symptoms elsewhere in the body.

The diagnosis of chronic prostatitis is made by rectal palpation and the finding of pus in the expressed prostatic secretion by microscopic examination.

The origin of the infection should be sought for carefully and eliminated. Prostatic massage with general hygiene, together with administration of a sulfonamide compound, usually will eradicate the infection, although prolonged treatment may be required.

Complications in the urinary tract are common and should also be treated to obtain the best results from local treatment to the prostate. Among the most frequent are urethral stricture, posterior urethritis and mild chronic renal infection.

Prostatic infection is so common and the prostate gland is so often the seat of a focus of infection that routine examination of this gland should be undertaken as frequently as that of the teeth and the tonsils.

Anesthesia.—Harbord[50] reports 94 cases in which spinal anesthesia was used for removal of the prostate gland. There were no deaths on the operating table, although 2 patients died on the day of operation. Twelve other patients died at intervals of two to twenty-six days after opera-

47. Huggins, C., and Bear, R. S.: The Course of the Prostatic Ducts and the Anatomy, Chemical and X-Ray Diffraction Analysis of Prostatic Calculi, J. Urol. **51**: 37-47 (Jan.) 1944.

48. Cristol, D. S., and Emmett, J. L.: The Incidence and Coincident Prostatic Calculi, Prostatic Hyperplasia and Carcinoma of the Prostate Gland, J. A. M. A. **124**:646 (March 4) 1944.

49. Henline, R. B.: Prostatitis and Seminal Vesiculitis: Acute and Chronic, J. A. M. A. **123**:608-615 (Nov. 6) 1943.

50. Harbord, R. P.: Spinal Analgesia for Prostatectomy: A Review of Ninety-Four Cases with Novocain Dissolved in the Spinal Fluid, Brit. J. Surg. **30**:235-237 (Jan.) 1943.

tion. In 6 per cent of the cases the anesthetic agent was unsatisfactory, necessitating secondary administration of gas and ether. The drug used was procaine hydrochloride in powdered form, and approximately 100 mg. was used in each case. The procaine was dissolved in the spinal fluid before administration.

URETHRA

Foreign Body.—Gutierrez [51] reports a case of an unusually long foreign body in the urethra, consisting of a crystal stirrer 16 cm. in length by 1 cm. in thickness, which was impacted firmly in the whole length of the penile-membranous portion and which necessitated open operation for its removal. The offending foreign body had caused painful priapism of seven days' duration, with severe dysuria and tenesmus, accompanied by balanitis, balanoposthitis and a gross amount of pus and blood in the voided urine. When a foreign body is impacted in the anterior portion of the penile part of the urethra, external urethrotomy must be performed on the glans penis. Since, however, plastic operations on the penile portion of the urethra have notoriously resulted in fistulas, one should, before their performance, institute a derivation of the urine by preliminary cystostomy in order to forestall infection and secure perfect healing. In the case reported by Gutierrez, the painful priapism was relieved by surgical removal of the offending foreign body from the urethra. The operation was carried out with ease and without bleeding. Two months after operation the wound was firmly healed, the voided specimen was clear and the urethra was permeable to a metal sound at 30 F.

In some cases in which the urethra is contaminated by an infected foreign body, it is wise after the external penile urethrotomy to leave the wound wide open. Even if the wound is closed one should not institute drainage by an indwelling urethral catheter. Drainage should be obtained instead by aseptic catheterization, carried out three or four times a day. In such cases a low protein diet, reduction of intake of fluid and control of the bowels by opiates for six days are useful measures. Granulation and healing of the wound will occur, in most cases, without infection by the end of the second or third week. The scar remaining in the glans penis is insignificant when the operation is properly done and does not cause any disturbance of normal sexual function. After any type of external urethrotomy the patient should receive dilations of the urethra with sounds up to 28, 29 or 30 F. as well as vesical irrigations and medical instillations for a considerable period, to secure patency and prevent strictures anywhere in its course.

Minor Lesions.—Ballenger, McDonald and Coleman [52] discuss disorders and lesions of the male urethra. They are due chiefly to inflammatory conditions, obstructions and hyperemia or hyperesthesia and manifest themselves chiefly as abnormal discharges, urinary irritation and sexual disturbances. Inflammation and obstructions are intimately related.

Strictures of the urethra, bottle necks in this urinary passageway, are of common occurrence. They may be congenital, acquired or both. The recognition of a narrow point in the urethra is so easy and so important that even the most casual examination, unless the urethra is acutely or subacutely inflamed, should include the introduction of bulbous bougies into the anterior part of the urethra. Obstructions of fairly large caliber may be associated with and cause a chronic "gleety" discharge, which will not clear up until after the stricture has been dilated. The same may be said of low backache and of postpubic or pelvic discomfort.

Low backache of male patients responds remarkably well to urethral dilation and massage of the prostate gland. Relief of low backache and pelvic discomfort often follows prostatic massage and the introduction of sounds, even when the prostatic secretion shows few or no pus cells and strictures of the urethra are not detectable. Among the patients suffering from low backache who come to urologists, 50 per cent or more will respond to prostatic massage and the appropriate use of sounds and medical instillations.

Occasionally, if the patient is a boy, instillations of 1 or 2 per cent solutions of silver nitrate into the deep portion of the urethra will be required after each treatment with the sound. If the patient is a boy, 1 or 2 per cent solution of intracaine (β-diethylaminoethyl-p-ethoxybenzoate hydrochloride) is injected into the urethra before the sounds are introduced.

Occlusion.—Dourmashkin [53] reports 5 cases of complete urethral occlusion of living newborn infants in which normal urination was established by creating a forced passage to the bladder with the aid of a whalebone filiform bougie and a small ureteral catheter. The occlusion involved the entire penile portion of the urethra in 2

51. Gutierrez, R.: Unusually Long Foreign Body Impacted in the Urethra, Causing Painful Priapism for Seven Days: Removal and Cure by External Urethrotomy, J. Urol. **49**:865-871 (June) 1943.

52. Ballenger, E. G.; McDonald, H. P., and Coleman, R. C.: Disorders and Lesions of the Male Urethra: Office Procedures, J. A. M. A. **123**:599-603 (Nov. 6) 1943.

53. Dourmashkin, R. L.: Complete Urethral Occlusion in Living Newborn: Report of Five Cases, J. Urol. **50**:747-755 (Dec.) 1943.

cases, the cavernous portion in 1 case, the prostatic portion in 1 case and the female urethra in 1 case.

Campbell [54] discusses stenosis of the external urethral meatus. In most cases in which the lesion is recognized the patients are children. In practically all of these cases it may be considered congenital, and it may also be congenital in adults. If the patient is an adult, recognition of the stenosis is most likely to coincide with attempted urethral instrumentation or acquisition of gonorrhea. Urographic study in these cases may be expected to reveal examples of advanced obstructive uropathy of the upper part of the tract wholly disproportionate to the commonly accepted benignity of meatal lesions. Campbell's report is based on a clinical study of 152 cases of which he had personal knowledge. The ages of the patients in this series ranged from 7 weeks to 16 years; a fourth were less than 24 months of age; half were between 24 months and 10 years. Twenty-six patients were girls.

Etiologically, stricture of the external meatus may be classified as congenital, 98 per cent or acquired, 2 per cent, by (*a*) trauma (indwelling catheter, instrumentation) or (*b*) infection (gonorrhea, nongonorrheal infection, vaginitis). Congenital stenosis is analogous to, and frequently accompanies, congenital stricture in the urethra proper, at the vesical neck or in the ureteral, intestinal or biliary tracts. In Campbell's experience, urethral stenosis commonly occurred with hypospadias (12 cases in this series) and is the urgent consideration; it also occurred in 1 case of epispadias and in 3 cases of congenital torsion of the penis. Acquired stenosis presenting the picture of sclerotic stricture may result from trauma or infection or the combination of these processes. This condition is observed chiefly among adults, particularly since the advent of transurethral prostatic resection and the more widespread employment of the indwelling catheter.

Pathologically, the changes due to back pressure are usually greatest in the bladder and next greater in the upper part of the urinary tract. Urinary infection was recorded in a fourth of Campbell's cases, in 16 of which the urologic examination was performed because of "chronic pyelitis." In some instances the dilatation is localized to the lower part of the urinary tract and particularly to the urethra.

Dysuria, frequency of urination and hematuria are the chief symptoms. Forty-nine of these patients were examined because of so-called persistent enuresis and 16 because of "chronic pyelitis." Not only is there hesitancy in starting the stream, but the stream itself is unusually small and the pressure generated to force the urine through the tight meatus will sometimes throw this fine stream 6 to 8 feet (1.8 to 2.4 meters). Chronic or recurrent vesical retention may be accompanied by leakage or overflow incontinence, and in 9 of Campbell's cases the obstruction produced abdominal pain.

Diagnosis is by inspection and is utterly simple; should diagnostic confirmation be needed, one should explore the stenosed meatus with a surgical probe or a small steel sound. When ulceration or incrustation of the meatus exists, its presence should suggest the diagnosis at once.

If the patient is male, Campbell's preference of treatment is liberal meatotomy with fine scissors or a small scalpel at the outset and subsequent periodic dilation of the stenosed meatus with steel sounds. If the patient is less than 1 year of age, the dilation is maintained up to at least 16 F. and for children from 2 to 5 years of age, up to 22 F. If the patient is female, instrumental dilation is preferable to meatotomy. At the time of the initial instrumentation, a small sound or bougie should be passed to the bladder to determine that there are no other congenital urethral obstructions. When possible, determination of the residual urine is of added value and is usually performed at the time of the initial visit and the meatotomy. If the patient is male, meatotomy and instrumentation are performed without anesthesia and usually in the office. Mucocutaneous suture of the meatus is not required.

Ulceration of the meatus may appear about the periphery of the stenosed meatus and usually extends 2 or 3 mm. within the opening. Although it does occur in uncircumcised boys (3 cases in this series), it is more common among boys who have been circumcised or whose short prepuce leaves the meatus well exposed. With drying of the ulcer, a scab or an incrustation forms, which further diminishes the meatal caliber or may seal the meatus completely between voidings.

PENILE ANESTHESIA

Magid and Culp [55] state that most of the popular types of local anesthesia for adult circumcision have failed to be entirely satisfactory. Ideal anesthesia of the entire penis and the anterior urethra is produced by injecting 10 cc. of 1 or 2 per cent solution of procaine hydrochloride containing 3 drops of epinephrine per

54. Campbell, M. F.: Stenosis of the External Urethral Meatus, J. Urol. **50**:740-746 (Dec.) 1943.

55. Magid, M. A., and Culp, O. S.: Ideal Penile Anesthesia Obtained by Injection of Corpora Cavernosa, J. Urol. **50**:508-513 (Oct.) 1943.

30 cc. into each corpus cavernosum just below the symphysis pubis. This type of local anesthesia is simple to administer, lasts three to seven hours, does not distort the penis, appears to be as safe as any other form of local infiltration and lends itself to many kinds of operative procedures on the penis and the urethra in addition to circumcision. It has been used by Magid and Culp on more than 300 patients with gratifying results and no toxicity.

TUMORS OF TESTICLE

Smith [56] reviews 50 cases of malignant tumor of the testicle. These include 2 cases of chorioepithelioma and 2 cases of bilateral tumor. Approximately twice as many growths occurred in the fourth decade of life as in any other decade. Gynecomastia and positive reactions to prolan tests proved to have little prognostic value. In 87 per cent of cases in which metastatic lesions developed, these lesions were discovered within two years after orchietcomy. Of 8 patients without metastatic lesions not treated by roentgen therapy 2 have lived more than four years. Of 23 patients without metastatic lesions treated by roentgen therapy 13 were in good health four or more years after operation. Many of the poor results followed incomplete irradiation of the abdomen, as metastatic lesions developed in regions that had not been treated. The ultimate results or roentgen treatment which had been postponed until metastatic lesions had developed were not good. Of 12 patients who had metastatic lesions, 3 responded well to irradiation. One of these has lived more than four years, 2 between two and three years. In cases in which metastatic lesions have developed, the thorax as well as the abdomen should be irradiated. The value of roentgen treatment is proved by the results obtained in this series of cases.

Morehead and Thomas [57] report data on a case in which cavernous hemangioma of the testicle probably originated from the tunica vasculosa of that organ. To their knowledge, this is the first case of hemangioma of the testicle recorded in the literature; furthermore, neoplastic growth has not been attributed previously to the tunica vasculosa. An inflammatory element complicated the neoplastic process. Edema, round cell infiltration and thrombosis were evident in certain regions of the tumor. The tumor had entirely replaced the testicle but was well differentiated, and surgical treatment should be followed by complete cure.

Warren and Olshausen [58] state that not enough is known of the normal variation of interstitial cells of the testicle to differentiate clearly pathologic states of these cells. On the negative side, there are certain helpful facts: Large collections of interstitial cells are not necessarily pathologic; multinucleated cells and cells in the tunica albuginea and epididymis do not necessarily indicate invasive growth, and cyclic changes of the number of interstitial cells from fetal life to senility tend to correspond inversely with changes in spermatogenesis.

Hyperplasia of interstitial cells associated with chronic diseases, injury, castration, cryptorchidism, changes of environment, ingestion of drugs in man, exposure to roentgen rays and radium, transplantation of testicles and administration of glandular extracts (chorionic gonadotropin and estrogens) and serum in animals may be due entirely or largely to diminished spermatogenesis. Of 29 reported cases of increase in number of testicular interstitial cells in human beings, including 4 cases reported by Warren and Olshausen, 12 were classified as cases of hyperplasia, 13 as cases of local tumor, 1 as a case of local tumor accompanied by hyperplasia and 3 as cases of malignant tumor.

Hyperplasia occurs principally at or after 45 years of age in atrophic testicles and is discovered chiefly at necropsy. Local tumors occur predominantly at or before 45 years of age in testicles larger than normal and are generally discovered during life and removed surgically.

Two of the three malignant tumors reported by Warren and Olshausen occurred before the patient was 45 years of age.

No definite criteria for diagnosing malignant lesions can be named, except for the presence of metastatic growths. However, if the testicle of a patient contains an increased number of interstitial cells, especially if the seminiferous tubules have been partially or completely destroyed, he should be carefully followed for more than ten years to watch for the appearance of metastatic growths if they are not present before that time.

INCONTINENCE

Counseller,[59] in discussing urinary incontinence of women, emphasizes the importance of a careful analysis of the cause of the incontinence and a complete understanding of the anatomy of the vesical neck, urethra and pelvic fascia plus

56. Smith, G. G.: Tumor of the Testicle: Analysis of the Results Obtained in Fifty Patients Treated by X-Ray Therapy, J. Urol. **50**:585-589 (Nov.) 1943.

57. Morehead, R. P., and Thomas, W. C.: Cavernous Hemangioma of the Testicle, J. Urol. **51**:72-74 (Jan.) 1944.

58. Warren, S., and Olshausen, K. W.: Interstitial Cell Growths of the Testicle, Am. J. Path. **19**:307-331 (March) 1943.

59. Counseller, V. S.: Urinary Incontinence in Women, Am. J. Obst. & Gynec. **45**:479-488 (March) 1943.

the normal physiology of micturition before undertaking any surgical corrective procedure.

Incontinence may be either congenital or acquired. Congenital incontinence is caused by a congenital defect, the extreme of which is represented by exstrophy of the bladder. Partial epispadias usually is the most confusing defect because in some instances the anatomic relations appear normal but on cystoscopic examination the musculature of the dorsal portion of the urethra is found missing.

Acquired incontinence is that incident to childbirth and less commonly that incident to operations for cystocele and prolapse. The incontinence may vary from moderate to severe, depending on the degree of trauma. Not all of these patients require cystoscopic examination, but a direct query regarding leakage of urine, when a vaginal plastic procedure or a vaginal hysterectomy is contemplated, is essential. Cystoscopic examination in cases of severe incontinence will reveal whether the urethra is distorted or the internal sphincter is gaping or fixed.

Counseller reports a series of 26 cases in which he performed the Kennedy operation for incontinence. In this procedure the cervix is grasped with a tenaculum and the anterior vaginal wall is opened in the usual manner to within 1.5 cm. of the external urinary meatus. The urethra is separated from the pubic rami on each side. This separation must be kept close to the bone to avoid a plexus of veins and branches of the inferior vesical artery and must extend into the paravesical space. If this is done gently, fibrous adhesions between the urethra and the pubic rami can be palpated and separated, with restoration of freedom of motion to the urethra. This freedom of motion must be maintained for complete relief of incontinence, and it is accomplished by plicating the tissues under the urethra by three mattress sutures, which hold the urethra from the pubic rami. A second row of mattress sutures picks up the edges of a fascia-like structure on the lateral surface of the urethra, and these sutures when tied separate the urethra farther from the pubic rami. An additional mattress suture should be placed to plicate the inner portion of the urethra about the internal sphincter.

The restoration of the voluntary sphincter is now done. The damaged portion of this muscle which remained attached to the vaginal wall is removed with the redundant portion of the vaginal wall which formed the urethrocele. The remaining intact sphincteral fibers are replaced by three no. 1 chromic catgut sutures. These sutures are passed through the vaginal wall close to the pubic rami, so as to be certain to catch the muscle fibers of the constrictor urethrae and the inferior layer of fascia of the urogenital diaphragm. When these are tied the edges are replaced beneath the middle and inner portions of the urethra. Kennedy uses silver wires instead of catgut. A male catheter is placed in the urethra for five to seven days or until the patient is out of bed, when she is advised to void as normally.

The result in all 26 of Counseller's cases was complete restoration of continence. Some patients contracted cystitis and urethritis of varying degrees, which induced some urinary urgency and frequency.

HERMAPHRODITISM

Lattimer, Engle and Yeaw [60] report a case of true hermaphroditism in a Negro, aged 11 years, who showed hypospadias and no palpable testes. On the right side a rudimentary ductus deferens, an epididymis and a juvenile testis were found in the abdomen. Structures resembling prostatic corpora amylacea were found where the prostate gland should have been. On the left side a rudimentary fused müllerian system emptied into the posterior urethra. In addition, there were a small ovotestis and a remnant of a fallopian tube on the right side. The ovary and the duct system were removed, and orchidopexy was performed. After a period of gonadotropic and androgenic hormone treatment, the hypospadias will be corrected.

UROLOGIC DIAGNOSIS

Bumpus [61] states, in a discussion of the indications for visual examination of the lower part of the urinary tract, that those who have personally undergone what in the surgical vernacular is termed a "cystoscopic examination" appreciate that, like the holy bonds of matrimony, it is not something to be undertaken lightly. The examiner who expects all his patients to fit a single cystoscope is to be censured. The dilation of urethras by sounds in order to make them fit cystoscopes, instead of using cystoscopes of suitable size, has caused much of the dread of this form of clinical investigation. Moreover, different cystoscopes are designed for different types of work, and the examiner who is not capable of utilizing the proper instrument handicaps himself and, by being thus handicapped, may fail to obtain the information most desired.

60. Lattimer, J. K.; Engle, E. T., and Yeaw, R. C.: True Hermaphroditism: A Case Report, with Interpretations, J. Urol. **50**:481-496 (Oct.) 1943.

61. Bumpus, H. C., Jr.: Indications for Visual Examination of Lower Urinary Tract, J. A. M. A. **123**: 615-617 (Nov. 6) 1943.

To reduce the discomfort of cystoscopy, the choice of anesthesia is naturally of importance. To carry out the procedure painlessly insures better cooperation on the part of the patient and assists in the acquisition of reliable information. It is comparatively easy to examine the interior of the bladder successfully when the patient is relaxed and free from pain. If the patient is female, a cotton applicator dipped in 10 per cent solution of cocaine and placed in the urethra for five or ten minutes before the passage of instruments has become a routine procedure. Two 2¼ grain (0.15 Gm.) tablets of cocaine dissolved in 1 fluidounce (30 cc.) of sterile water immediately before injection into the male urethra has proved in many thousands of cases to produce the most efficient local anesthesia.

To infect a normal urinary tract it is necessary to traumatize it. Experiments have shown that its exposure to bacteria without trauma will not cause infection. The passage of instruments is a common cause of trauma. Infection should be avoided by first filling the urethra with a suitable lubricant or lubricating the instrument thoroughly and then passing it with great care and gentleness. A more frequent cause of trauma is the overdistention of the bladder, resulting in spasm. The instrument may be passed with skill, but when the bladder is filled beyond comfort trauma is produced, which in the presence of infection will be followed inevitably by fever and chills. When the examiner has discovered a pathologic process in the urinary tract, nothing but added trauma is gained by long-continued observation.

With the advent of intravenous urography, it seemed for a time that need of instrumental examinations, particularly the passage of ureteral catheters, would be curtailed greatly. This has not proved to be the case. The unsuspected pathologic condition that has been revealed by the general use of intravenous pyelography has made evident the need for supplementary information. This can be obtained only by ureteral catheterization and visual examination of the lower part of the urinary tract. Unless all possible information from all possible sources is at hand, both diagnosis and treatment are of doubtful validity.

Ballenger,[62] in discussing indications for visual examination of the lower part of the urinary tract, protests against the routine cystoscopic study of the prostate and the prostatic portion of the urethra of elderly men. In the majority of instances in which urinary obstruction is the chief symptom, adequate facts may be obtained without cystoscopy. By rectal palpation the size and the consistency of the prostate gland may be ascertained easily. A roentgenogram will show whether or not stones are present, and a cystogram will demonstrate the amount of intravesical protrusion of the prostate as well as the diverticula, if present. Beyond the information gained from these studies little else is required except a general physical examination, urinalysis, tests of renal function and examination of the blood. Cystoscopy when the prostate is hypertrophied is likely to bring on acute retention of urine, even among uninfected patients. Among such patients the disturbing reactions are often more severe than those after transurethral resection of the obstructing prostate.

Bumpus [63] states that, because it is one of the most exact of clinical specialties, an accurate urologic diagnosis frequently can be obtained by several different methods. It does not follow, however, that more than a single method need be employed. Once a diagnosis of a tuberculous infection in a kidney is confirmed by the finding of acid-fast bacilli in the urine from it or extensive hydronephrosis is discovered by withdrawal of its contents, it is not imperative to make a pyelogram as confirmatory proof of what is already a known fact, since unnecessary examination may add not only to the cost but to the risk of investigation. Miliary tuberculosis has followed pyelography, and septicemia has followed overdistention of a renal pelvis.

McKim, Smith and Rush [64] review data on 152 cases of dysuria and nocturia in female patients whose urine was normal.

One of the most frequent causes of symptoms is the urethral caruncle. The examining physician must not be misled by normal external conditions. Many caruncles are located immediately behind a rigid meatus of small caliber. This "intraurethral" type is more prevalent than the external type and may be overlooked easily unless the following technic is used routinely: Insert in the meatus a small cotton swab saturated with 10 per cent solution of cocaine and allow it to remain five minutes. Then by gentle traction on the swab the intraurethral caruncle, if present, can be pulled forward to the external orifice, and its size, shape and location in the meatus can be noted. In several instances the contracted meatus necessitated dilation before the growth could be demonstrated on the inner surface of the urethral mucosa immediately behind the dilated orifice.

In an earlier reported series of 202 cases of urethral caruncle, the following observations in

62. Ballenger, E. G., in discussion on Bumpus,[61] p. 618.

63. Bumpus, H. C., Jr., in discussion on Bumpus,[61] p. 619.

64. McKim, G. F.; Smith, P. G., and Rush, T. W.: Dysuria and Nocturia in the Presence of Normal Urine in the Female, J. A. M. A. **123**:603-607 (Nov. 6) 1943.

the urinary tract were noted: Urethral strictures were present in 8 cases; the strictures were located immediately adjacent to the caruncles, and all the patients gave histories of previous applications of cauterizing solutions. Urethritis was present in 81 cases in which there were varying degrees of easily recognizable urethral inflammation. In 54 cases of cysts of the vesical orifice cystic degeneration of the mucosa of the vesical orifice was demonstrated easily. In 111 cases the urine in the bladder showed infection, both acute and chronic. In 20 cases the bladder was contracted to a capacity of less than 6 fluid-ounces (180 cc.). In 2 cases interstitial cystitis was found and in 2 cases bilateral pyelonephritis. As a result of the frequency with which involvement of the urinary tract above the caruncle was demonstrated in this series, it was concluded not only that urethral caruncles should be regarded as an important etiologic factor in the production of vesical symptoms but that in many cases they act as true obstructions to the urinary outflow and produce the complications of urinary obstruction.

It is a fact acceptable to most urologists that the female urethra harbors numerous organisms, the so-called fossa navicularis being the chief receptacle.

In accordance with surgical principles of treating inflammatory lesions in other organs of the body, an inflamed bladder is let alone temporarily unless an emergent condition demands further investigation.

Rest in bed is advised, with at least eight to ten glasses (1.9 to 2.4 liters) of water in the twenty-four hour period and a soft diet, with no fruit juices. The patient is given twenty-eight 7½ grain (0.48 Gm.) tablets of sulfathiazole and instructed to take one tablet after meals and at bedtime.

Visualization of the interior of the bladder by cystoscopy was done in each of the 152 cases. Frequently a combination of two or more etiologic factors was found in the same case, such as pelvic abnormality and urethral cysts or intramural cystitis.

Moore [65] states that there exists a widespread tendency to underestimate the importance of symptoms referable to the bladder among women when examination of the urine gives negative results. An accurate estimate of the condition of the urethra is not at all a complicated procedure if an endoscopic view is obtained. Lesions involving the urethra may be overlooked easily with the average indirect vision cystoscope. It has been Moore's experience that chronic nonspecific urethritis of women is often refractory to treatment and in such cases palpation of the urethra with a sound in place will often reveal small shotlike infiltrations due to chronic inflammatory changes in the periurethral glands. Massaging the urethra lightly over the sound, preferably after instillation of a mild antiseptic, may hasten recovery. Gradual and gentle dilation of the urethra also has been of definite value and is attended by a minimum of trauma if a rubber-covered Kollmann dilator is employed. Dilations given at intervals of ten days to two weeks may be carried finally to 35 or 40 F. Chronic interstitial cystitis, or panmural fibrosis, is the most stubborn condition to eradicate of all the entities mentioned in Moore's article. Patients who do not respond to hydraulic distention, treatment with silver nitrate or light electrocoagulation and who have sufficiently distressing symptoms should be considered possible candidates for presacral neurectomy.

One of the common causes of vesical symptoms encountered in this series was cystic degeneration of the mucosa of the vesical orifice. This condition was noted in 70 cases. These cysts can be described as appearing in a variety of forms and may be classified as single or multiple, bullous or pedunculated.

The bullous type was encountered in 26 cases and appeared as superficial, rounded elevations beneath a thin urethral mucosa, which was more or less distorted by associated edema and congestion and resulted in the formation of folds of mucous membrane with intervening clefts. It is interesting to note that in 16 of these cases not only was the urine free from infection but there was no residual urine. In the remaining 10 cases varying amounts of residual urine were found. The cystoscopic findings in the 44 cases in which the pedunculated type predominated were entirely different. In several cases the cysts were located inside the vesical orifice adjacent to the trigone and in others they were found in the urethra just outside the sphincter.

Urinary symptoms varied in different cases, though frequency was recorded in all. In most cases, particularly in those in which there was no residual urine, frequency was aggravated while the patient was on her feet.

Selected patients suffering from these lesions were treated in the office, although the most satisfactory and permanent results have been obtained when the patient was hospitalized. With the patient under light anesthesia, preferably low spinal, the lesions are treated by direct application under vision with the high frequency spark, it being necessary not only to cauterize the base of the protruding cyst but to cauterize gently all of the mucosa of the vesical orifice.

65. Moore, T. D., in discussion on Bumpus,[61] p. 618.

URINARY EXTRAVASATION

Finestone [66] reviews data on 32 cases of urinary extravasation, in 16 of which the patient died. Of 3 patients on whom operation was not performed, all died. Of 11 patients on whom suprapubic cystotomy was performed, 7 survived. Of 9 patients on whom external urethrotomy was performed, 6 survived. Of the 9 patients on whom operation was performed without any diversion, only 3 survived. In 2 of the last 3 cases, there were only localized conditions resembling periurethral abscess. In the third case the perineum ruptured spontaneously, thereby adequately diverting the urinary stream and saving the patient's life.

In the last 7 consecutive cases in the latter part of 1938 and 1939, when the principles discussed later were emphasized, there were no deaths.

Operative intervention is essential and is always an emergency procedure. Spinal anesthesia gives the lowest mortality rate. Besides multiple incisions of infiltrated tissues, diversion of the urinary stream is of paramount importance. Diversion of the urinary stream is accomplished by one of three methods: suprapubic cystotomy, external urethrotomy or indwelling urethral catheter (which is condemned). Multiple incisions should be short and superficial. There is no necessity for exposing the testes; unnecessary mutilation is thereby avoided. The general condition requires strenuous measures: continuous intravenous infusions, transfusions and administration of tetanus and anaerobic antitoxin, gas gangrene antiserum and sulfonamide compounds.

URINARY ANTISEPSIS

Helmholz,[67] in discussing the effects of various urinary antiseptics on strains of Escherichia coli, states that resistance to sulfathiazole is manifested by a small percentage of strains of E. coli. The size of the inoculum of bacteria may determine the presence or absence of bactericidal action. Strains resistant to sulfathiazole were also resistant to urinary acidity and mandelic acid but were more susceptible to methenamine and methenamine mandelate than nonresistant strains. Sulfathiazole and sulfadiazine seem to be more effective against E. coli than sulfacetimide, sulfapyridine or sulfanilamide. In concentrations of 0.5 mg. per hundred cubic centimeters sulfathiazole is more effective than sulfadiazine.

ORTHOSTATIC ALBUMINURIA

Prince [68] reports the case histories of 5 young men who had been rejected from military duty because of albuminuria. Four of these patients were proved to have orthostatic albuminuria and have since been accepted by medical examining boards for active duty with the armed forces. The fifth patient was found not to have orthostatic albuminuria and is included in this series as an excellent example of the careful studies which are necessary before this diagnosis should be made.

The various studies and examinations which were performed to determine the correct diagnosis in these cases are reported carefully and are described in such a manner that they may be repeated easily by any physician interested in similar cases of albuminuria among apparently healthy young persons.

The criteria which should be met before a diagnosis of orthostatic albuminuria is made are given and are discussed in some detail. The various "lordotic" tests are described fully, and the importance of intravenous urograms in these cases is emphasized.

Orthostatic albuminuria is a rather common condition, which is quite harmless and which usually disappears shortly after puberty and practically always by the end of the third decade of life. It does not have any effect on general health or longevity. The diagnosis of orthostatic albuminuria requires careful and thorough examinations of various types. The condition must not be confused with chronic glomerulonephritis in a latent stage.

Albuminuria of this type does not require any treatment, and curtailment of activity in this condition is contraindicated. There is no reason why young persons who have orthostatic albuminuria should not be allowed to serve with the armed forces.

SULFONAMIDE DRUG THERAPY

Sobin, Aronberg and Rolnick [69] state that intrarenal foreign material following sulfonamide drug therapy is of two types: (1) precipitated sulfonamide compounds and their acetylated

66. Finestone, E. O.: Urinary Extravasation (Periurethral Phlegmon): A New Concept of the Pathogenesis and the Treatment, New York State J. Med. **43**:1320-1324 (July 15) 1943.

67. Helmholz, H. F.: Effects of Various Urinary Antiseptics on Strains of Escherichia Coli: I. Sulfathiazole; II. Urinary Acidity, Mandelic Acid, Methenamine and Methenamine Mandelate; III. Relative Value of Sulfathiazole, Sulfadiazine, Sulfapyridine, Sulfacetimide and Sulfanilamide, Am. J. Dis. Child. **65**:399-411 (March) 1943.

68. Prince, C. L.: Orthostatic Albuminuria, J. Urol. **50**:608-620 (Nov.) 1943.

69. Sobin, S. S.; Aronberg, L. M., and Rolnick, H. C.: The Nature of the Renal Lesion with the Sulfonamides and Its Prevention with Urea, Am. J. Path. **19**:211-223 (March) 1943.

products; (2) cellular debris, with deposition of calcium and iron around or on this material. Urea simultaneously administered with sodium acetylsulfapyridine will prevent the precipitation of sulfonamide compounds and the formation of renal calculi in rats. The action of urea is independent of a diuretic effect and depends on a specific solvent effect on acetylsulfapyridine. The nephrotoxic properties of acetylsulfapyridine are mechanical and result from precipitation of the drug in the renal tract. Calcification in the kidney and resultant formation of calculus in animals treated with sulfonamide drugs are dependent on local damage to tissue and secondary deposition of calcium and iron on focal, nonviable structures.

La Towsky [70] presents the results of treatment with sulfadiazine on 100 patients with nonspecific infection of the urinary tract. Most of the patients received from 2 to 4 Gm. of sulfadiazine per day for four to sixty days. In general, infection of the urinary tract of patients who had benign prostatic hypertrophy, cystitis secondary to stricture, prostatitis, nonurinary operation, calculous and noncalculous pyelonephritis and epididymitis showed a satisfactory response. Patients who had infections of the urinary tract associated with adenocarcinoma of the prostate, vesical tumor and vesical diverticulum did not respond satisfactorily. All species of pathogens of the urinary tract encountered in this series of patients responded in greater or lesser degree to administration of sulfadiazine. The results of treatment of nonspecific infections of the urinary tract with sulfadiazine in this series compare favorably with the reports of the action of sulfathiazole on such infections found in the literature.

Campbell and Fobes [71] report a case of sulfadiazine anuria in which, the establishment of urinary drainage by ureteral catheterization having failed, for technical reasons, the life of the moribund patient was saved by unilateral ureteropyelostomy. The restoration of isolateral renal function was immediate. When anuria occurs during treatment with a sulfonamide compound and conservative noninstrumental and instrumental treatment is fruitless within forty-eight hours, surgical drainage of at least one kidney should be instituted without delay. This offers the remaining hope for saving the patient's life, for, with the return to unilateral renal function, uremia disappears and at a suitable subsequent time—preferably within seven to ten days—cystoscopic efforts to unblock the opposite upper urinary channels can be made. If the unilateral operation fails to promote free urinary drainage within twelve to twenty-four hours, one should promptly and surgically drain the opposite kidney.

Mathé [72] states that administration of sulfadiazine is accompanied by few side reactions; yet serious renal complications including anuria and death ensue with relative frequency. The prolonged, comparatively nontoxic effect of the drug on the gastrointestinal tract is no criterion for determining the absence of renal damage. Two types of sulfadiazine anuria are encountered: mechanical, due to blockage of the upper or lower part of the urinary tract with crystalline deposits; chemical, due to acute toxic degenerative nephritis caused by calcifying necrosis. The danger signals of impending anuria are hematuria, oliguria, azotemia and renal tenderness accompanied by flatulence, nausea and vomiting.

Prophylactic treatment consists in reducing the dose of the drug to a maximum of 4 Gm. a day, maintaining the blood level below 8 mg. per hundred cubic centimeters, forcing fluids to a daily urine output of 1,200 to 1,500 cc. and alkalizing the urine to a sustained p_H of 7.5. In the presence of anuria administration of the drug should be discontinued and ureteral catheterization and pelvic lavage, or in some cases nephrostomy drainage, should be performed. No apparent permanent renal damage has been observed among patients relieved of sulfadiazine anuria.

Mathé reports a case of mechanical sulfadiazine anuria, which occurred seven days after administration of 15 Gm. of sulfadiazine for acute bronchitis to a patient presenting bilateral ureteral stricture. The anuria was relieved by ureteral catheterization and pelvic lavage.

ADRENAL TUMORS

O'Crowley and Martland [73] state that adrenal-renal heterotopia with adrenal glands (complete heterotopia) or a considerable portion of them (partial heterotopia) beneath the capsule of the kidneys and with no adrenal glands in their normal position is not as uncommon as the literature indicates. O'Crowley and Martland

70. La Towsky, L. W.: The Clinical Use of Sulfadiazine in Nonspecific Urinary Tract Infections—A Study of One Hundred Cases, J. Urol. **50**:625-631 (Nov.) 1943.

71. Campbell, M. F., and Fobes, J. H.: Sulfadiazine Anuria: Its Relief by Ureteropyelostomy, Am. J. Surg. **61**:99-102 (July) 1943.

72. Mathé, C. P.: Sulfadiazine Anuria Due to Mechanical Blockage of the Ureters by Crystalline Deposits: Report of a Case, Urol. & Cutan. Rev. **47**:168-171 (March) 1943.

73. O'Crowley, C. R., and Martland, H. S.: Adrenal Heterotopia, Rests, and the So-Called Grawitz Tumor, J. Urol. **50**:756-768 (Dec.) 1943.

have encountered this condition eight times in the routine examination of 5,000 consecutive bodies.

The explanation of this anomaly, which in O'Crowley and Martland's experience is always bilateral, is unknown. As the renal capsule is said to be completed at a time in early fetal life when the adrenal cortex is far distant, it would seem that a mechanical displacement is impossible. It suggests that embryologic data are incomplete, that exceptions occur or that pluripotent cells exist which can form either renal parenchyma or adrenal cortex.

Contrary to some authorities, this anomaly seems not to have any effect on the life of the patient. In the experience of O'Crowley and Martland, it neither shortens life nor predisposes to infections, tuberculosis or debilitating diseases. No endocrine disturbances were observed.

The recorded high incidence of status lymphaticus with this anomaly is not borne out in this series of cases.

In cases of adrenal-renal heterotopia the surgeon in performing nephrectomy would remove the adrenal gland unwittingly. Since the heterotopic glands are hypoplastic and in addition do not contain any medulla (or scant medulla in extracapsular portions only), such an operation might cause symptoms suggesting adrenal insufficiency.

Finally, the demonstration that the entire adrenal cortex, or large portions of it, may be found beneath the renal capsule remaining on the kidney after decapsulation and the finding in some of these cases of many small, isolated bits of cortical tissue near these subcapsular adrenals, but scattered over the surface of the kidney, greatly strengthen the opinion held by many pathologists that the so-called adrenal rests are bits of cortical adrenal tissue which have become misplaced during development.

It is reasonable to assume, therefore, that some renal hypernephromas may arise from such misplaced cortical adrenal tissue.

The only other explanation would be the concept that pluripotent cells exist which may give rise to any of these structures. There is no way of refuting such an argument.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1943

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

I. CONGENITAL DEFORMITIES

PREPARED BY J. HIRAM KITE, M.D., ATLANTA, GA.

Only about one eighth of the average number of articles on congenital deformities have appeared during the past year.

Of the work that has been reported, I place that of Warkany and his associates first.[1] They state that it is desirable to prevent rather than to treat congenital defects. This desire has kept alive among physicians a definite interest in research concerned with the causes of malformations. Apparently a great variety of factors can interfere with the normal development of the embryo. During the last few decades the discovery of genetic factors which produce malformations has attracted a great deal of attention, while research in the field of environmental teratogenic factors, in mammals at least, has lagged. However, some important discoveries made in recent years promise to renew interest in the environmental factors. It is of special interest that in several instances a relationship has been found between a faulty maternal diet and anomalies of the offspring. Franke and Tully have described the development of malformations in chick embryos the mothers of which were fed grains containing selenium. With the recognition of the importance in nutrition of trace substances, particularly vitamins, it appeared possible that a qualitative maternal dietary deficiency could cause abnormal intrauterine development of the embryo or fetus.

Warkany and Nelson in 1940 described the appearance of skeletal abnormalities in the offspring of rats reared on a deficient diet. They found the frequency of osseous defects in 100 cleared abnormal specimens to be as follows:

Tibia 93	Hand 54	Maxilla 8
Mandible ..80	Sternum ...52	Scapula 6
Ribs 75	Ulna 50	Clavicle 6
Fibula 63	Humerus ..34	Femur 1
Radius 58	Hindfoot ..31	

In summarizing their study they say that congenital malformations induced in rats by maternal nutritional deficiency date back to the cartilaginous or precartilaginous stage of the structures affected. The defects of ossification are secondary results, caused by faulty development of the precursors of the bones. Many cartilaginous structures show a lack of division in the longitudinal and transverse direction; this leads to a reduction in the number of skeletal elements and to syndactylism and brachydactylism in the paws. The radius, ulna, tibia and fibula are frequently shortened in the cartilaginous stage. Ossification is delayed and faulty, and eccentric centers of ossification lead to an abnormal arrangement of the trabeculae of the bones.

Hilliard[2] reports a case of chondro-osseous dystrophy with punctate epiphysial dysplasia. The infant had short upper arms with relatively large spadelike hands and flexed fingers. The humerus on both sides was short and thick, with splayed ends. The elbow joint had grossly irregular epiphyses. The radius and the ulna were normal in length, and the metacarpal bones were larger than normal, with an hourglass appearance, and contained denser areas at the ends. The femurs were short and thick, with condyles presenting a balloon appearance. The patellas had a stippled appearance, due to a punctate dense ossification. The tibia and the fibula were normal in proportions but showed dense areas in the upper and lower ends. Just above the lower end of the tibia, fibula, radius and ulna there was a zone of diminished density. He says that the work of Harris shows that this deformity is really an example of a fundamental deficiency in cartilage; the extreme condition is achondroplasia, and the least abnormal is congenital dislocation of the hip, which is probably due to a failure to maintain the hereditary form of the epiphysis, as a result of mucoid degeneration of the cartilage.

Resnick[3] reports 3 cases of hereditary dyschondroplastic genu varum. He says that dyschondroplasia is a retardation of the normal

1. Warkany, J.; Nelson, R. C., and Schraffenberger, E.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, J. Bone & Joint Surg. **25**:261 (April) 1943.

2. Hilliard, C.: Chondro-Osseous Dystrophy with Punctate Epiphyseal Dysplasia, Brit. J. Radiol. **16**:144 (May) 1943.

3. Resnick, E.: Hereditary Dyschondroplastic Genu Varum, J. Bone & Joint Surg. **25**:202 (Jan.) 1943.

transformation of primordial cartilage into growing bone, which results in irregularity of ossification at the epiphysial-metaphysial junction of the long bones. The first case was described by Ollier in 1899. Since that time, many cases have been reported in the literature, and recently there have been several articles describing dyschondroplastic bow legs. He reports the cases of a mother, a daughter and a son with extreme bow legs.

Resnick [4] also reports the case of an Italian mother and identical male twins with epiphysial dysplasia punctata. All 3 showed roentgenographic evidence of multiple osteochondritis with underdevelopment of the epiphyses, not associated with a definite hypothyroid state. No symptoms were associated with the osteochondritis except those of the hip joints. At the time this report was written, the mother had deformed femoral heads and necks, which caused pain and a limp. One child, in whom epiphysial changes left a deformed head and neck of the femur, also had moderate pain on active use, while the other child, whose left upper femoral epiphysis regenerated so that normal contour resulted, was free of symptoms.

Chondrodystrophia calcificans congenita is discussed by Raap,[5] who reports 4 cases. This rare condition was first described by Conradi in 1914. The deformity has been reported under varied names, with a tendency toward the name chondroplasia. Raap thinks, however, that the term chondrodystrophia appears more logical and has added the two descriptive adjectives. He studied roentgenograms of a 10 month old twin with a thoracic condition and found a mottled granular appearance in the ankles, wrists and other joints, which in contour followed the bony structures with normal ossification but presented angular densifications rather than rounded densities. The other twin, who had just died of pneumonia, was exhumed and found to have changes in the joints like those of the living twin. Microscopic sections from the dead twin showed an increase of fibrous tissue of periosteal character. Directly under this periosteum a formation of cartilage was noted. The deeper cells were acquiring a cartilaginous character. The deepest layers of cells formed osteoid tissue, which was partly calcified. The parents showed normal bony structures in these areas. A baby born two weeks later showed the same deformity, and a 2½ year old sister showed the remains of this same condition. He says that these abnormal calcifications are marked at birth and disappear by the age of about 3 years. All chemical and other studies on the blood gave normal results, and there was no evidence of dwarfism, cretinism, rickets or scurvy.

Arthrogryposis multiplex congenita is a term used to designate contractures of the joints. The term "arthrogryposis" is a combination of two Greek words, meaning literally a crooked or bent joint. Katzeff [6] reports briefly 18 cases from the Children's Hospital in Boston. She says that the extremities lack the usual anatomic contours, having instead a stuffed-sausage-like appearance. Little muscle is palpable. The structures overlying the joints feel thickened and contracted. Dimples are frequently seen over the patellas and elbows. In most of the involved muscles passive correction of the contractures is possible to a few degrees, although some are rigid, allowing no correction. These gross abnormalities are symmetric, distinctive and readily recognizable. Histologically there are atrophy and fatty replacement of the involved muscles. The younger patients are treated by manipulations, with or without anesthesia, supports and surgical corrections. The older patients are treated by fasciotomy, capsulotomy, lengthening of tendons, open reduction of hips and arthrodesis for the correction of clubfoot. "These badly disabled children, presenting at birth a discouraging picture, were definitely improved by treatment."

[Ed. Note (J. H. K.).—A report on this interesting subject would have been more helpful to the reader who was not familiar with arthrogryposis if the writer had made a more detailed analysis of the cases. She states that the feet were "involved," without any mention of the types of deformity present. In my experience the common deformity is an atypical clubfoot. Naming the types of treatment used fails to tell the entire story of the treatment of this condition. From this article one would get the impression that the treatment is easy and sure. Any one having extensive personal experience with arthrogryposis would say that it is one of the most discouraging congenital deformities to treat. It is important from the standpoint of treatment that an early diagnosis be made, but it is much more important that the nature of the condition be recognized and that it be explained to the parents, so that they will not expect the good results in these stiff joints which they have seen in stiff joints not associated with arthrogryposis. This explanation will save much embarrassment later.

4. Resnick, E.: Epiphyseal Dysplasia Punctata in a Mother and Identical Male Twins, J. Bone & Joint Surg. **25**:461 (April) 1943.

5. Raap, G.: Chondrodystrophia Calcificans Congenita, Am. J. Roentgenol. **49**:77 (Jan.) 1943.

6. Katzeff, M.: Arthrogryposis Multiplex Congenita, Arch. Surg. **46**:673 (May) 1943.

The prognosis is so bad for this condition that I have often questioned the wisdom of spending a large amount of charity funds on children with this deformity. The treatment requires a much longer time than is usually expected, and the tendency to recur is much greater. No statement is made in this report about recurrences. The strong tendency to recur is one of the outstanding features of the condition. None of my patients held the correction obtained by the first course of treatment. They all returned for more treatment at a later date. The statement is made that open reduction of the hips was used, but the final results are not mentioned. In my cases the stiff hips which could not be moved with the patient under anesthesia were allowed to remain dislocated, since they were stable, and they do not seem to be any the worse for it.]

II. DISEASES OF GROWING AND OF ADULT BONE

PREPARED BY JOHN A. SIEGLING, M.D., CHARLESTON, S. C.

Few of the conditions in this section have any relationship to military combat, but a review of the literature for the year reveals a number of previously unreported cases of diseases of bone in selectees.

Growth of Bone.—From a study of 84 children, Sontag and Lipford [7] conclude that acute disease does not materially affect the appearance of centers of ossification. This is at variance with the work of Francis and Todd.

Lurie, Levy and Lurie [8] present a method of determining the age of bone which is simpler and more practical than previous methods but which is still somewhat complicated. The method is based on graphs on which is recorded the average time of appearance and fusion of epiphyses. Since this time varies in boys and girls, two graphs are given. Four roentgenograms are then taken for each person—one of the hand, including the wrist, one of the elbow, one of the pelvis and one of the foot, including the ankle. By using the two graphs in conjunction with the chronologic age, the normal age of the bones can be determined, and by comparing the roentgenograms of the child with the norm, it can be ascertained whether or not the age of the bones is accelerated or retarded.

Disease of Bone Due to Decompression.—Allan,[9] in an interesting paper, calls attention to the essential similarity of lesions of bone in caisson disease and lesions of bone as a result of decompression in high altitude flying. He states that in an ascending airplane the pressure of nitrogen in the lungs falls and nitrogen is released in the blood in the form of bubbles, which produce emphysematous and embolic symptoms. The article calls attention to the fact that the favorite areas for lesions of bone are the long bones and the shoulder and hip joints. Articular lesions are frequent. Roentgenograms reveal well defined mottled areas of increased density involving the medullary portions of the diaphysis and producing no cortical changes. The articular lesion is represented by mottled changes of irregular ossification in the head of the femur or humerus, with flattening of its articular surface, irregularity and narrowing of the cartilage space and marginal lipping.

The author stresses the importance of recognizing the clinical and roentgenographic features of this disease, with its ultimate relationship to possible claims for compensation. It is of paramount interest in time of war, as the incidence of illness caused by decompression increases with high altitude flying.

Aseptic Necrosis.—The clinical and roentgen diagnosis of this osseous condition is now generally recognized. Lewis [10] gives a brief summary of the pathologic and roentgenographic observations in post-traumatic aseptic necrosis, stressing the importance of early diagnosis. Brailsford [11] emphasizes the belief that there is a period of from one to four years during which necrotic bone is plastic and during which it should be protected from stress and strain while resubstitution is occurring.

Thyroid Gland.—Subsequent to the publication of the report of Cavanaugh, Shelton and Sutherland in 1936, concerning the evidence of metabolic (thyroid) deficiency in 5 cases of Legg-Perthes disease, a great many persons have used thyroid in its treatment. Gill [12] re-

7. Sontag, L. W., and Lipford, J.: Effect of Illness and Other Factors on the Appearance Pattern of Skeletal Epiphyses, J. Pediat. **23**:391-409 (Oct.) 1943.

8. Lurie, L. A.; Levy, S., and Lurie, M. L.: Determination of Bone Age in Children, J. Pediat. **23**:131-140 (Aug.) 1943.

9. Allan, J. H.: Decompression Disease of Bone, J. Aviation Med. **14**:105-111 (June) 1943.

10. Lewis, R. W.: Post-Traumatic Necrosis of Bone, Am. J. Roentgenol. **49**:593-599 (May) 1943.

11. Brailsford, J. F.: Avascular Necrosis of Bone, J. Bone & Joint Surg. **25**:249-260 (April) 1943.

12. Gill, A. B.: Relationship of Legg-Perthes' Disease to the Function of the Thyroid Gland, J. Bone & Joint Surg. **25**:892-901 (Oct.) 1943.

ports a careful study of 20 cases of Legg-Perthes disease, which controverts this previous report.

Jacobs [13] reports 2 cases of juvenile hyperthyroidism in which there was osteodystrophia fibrosa cystica with diffuse osteoporosis complicated by pathologic fractures. One of the patients recovered after thyroidectomy, and the other, who had not been operated on, remained toxic. The condition simulates von Recklinghausen's disease closely.

Osteitis Deformans.—Reports of sarcoma associated with Paget's disease continue to filter into the literature, and the frequency of the association is more than casual. In different reported series, the incidence varies from 6.1 per cent to 14 per cent. Kirshbaum [14] reports a case of giant cell fibrosarcoma of the skull associated with Paget's disease and states that every case of sarcoma of the skull should be investigated for the coexistence of Paget's disease. Pike [15] reports 3 cases of osteogenic sarcoma in patients with Paget's disease, and Campbell and Whitfield [16] report 3 cases of vertebral sarcoma secondary to Paget's disease. Strachstein [17] calls attention to the possibility of mistaking osteitis deformans for metastatic prostatic carcinoma, and the converse. Symmetric involvement is usual; clinically, however, mono-osteitic Paget's disease certainly exists. Groh [18] reports 9 cases with roentgenographic proof of its localized existence. It is felt, however, that the evidence in these cases is somewhat inconclusive, as it is not substantiated by pathologic study.

Fragilitas Ossium.—Interest continues in this obscure disease for which no treatment has yet been suggested. Bickel, Ghormley and Camp [19] report a study of 40 cases of this condition, which, on a basis of family history, can be classified into a hereditary and a nonhereditary, or congenital type. Farber and Margulis [20] have traced a family of 52 members through four generations, 12 of whom had been affected with fragilitas ossium. The series illustrates the hereditary character of the disease, and the authors state that the most constant feature of the condition is scleral imperfection. In this series males and females were equally affected and deafness occurred in 4 cases.

Brailsford [21] reports 9 cases of various types of osteogenesis imperfecta.

Parathyroid Glands, Renal Insufficiency and Bony Changes.—Increasing emphasis is being placed on changes in bones associated with renal insufficiency. Follis and Jackson [22] studied sections from vertebrae of 39 persons who had died of renal insufficiency and found histologic changes in 50 per cent. Excessive osteoid was the principal abnormality rather than osteitis fibrosa.

Soffer and Cohn [23] carefully differentiate primary and secondary hyperparathyroidism, stressing the presence of adenoma in the primary condition and hyperplastic glands, with or without characteristic osseous changes, in secondary hyperparathyroidism. Secondary hyperparathyroidism may occur in patients with chronic renal disease, multiple myeloma, carcinomatous metastasis to bones, Cushing's syndrome, rickets and osteomalacia. The most common cause of secondary hyperparathyroidism is chronic renal disease. Curtis and Feller [24] report a case which illustrates that sometimes primary hyperparathyroidism resulting in renal damage and primary renal disease resulting in hyperparathyroidism may so resemble each other in their respective terminal stages as to be indistinguishable either clinically or at postmortem examination.

A great deal of interest has been evinced in the association of osteitis fibrosa cystica with tumor of the parathyroid gland if the number of case reports can be taken as an index. Orr [25] reports a case in which the cysts of the bones

13. Jacobs, J. E.: Osteodystrophia Fibrosa Cystica and Juvenile Hyperthyroidism, South. M. J. **36**:668-673 (Oct.) 1943.

14. Kirshbaum, J. D.: Fibrosarcoma of the Skull in Paget's Disease, Arch. Path. **36**:74-79 (July) 1943.

15. Pike, M. M.: Paget's Disease with Associated Osteogenic Sarcoma, Arch. Surg. **46**:750-753 (May) 1943.

16. Campbell, E., and Whitfield, R. D.: Osteogenic Sarcoma of Vertebrae Secondary to Paget's Disease, New York State J. Med. **43**:931-938 (May 15) 1943.

17. Strachstein, A.: Carcinoma of the Prostate: Pitfalls in Diagnosis, with Report of Two Cases, J. Urol. **49**:118-124 (Jan.) 1943.

18. Groh, J. A.: Mono-Osteitic Paget's Disease as a Clinical Entity, Am. J. Roentgenol. **50**:230-243 (Aug.) 1943.

19. Bickel, W. H.; Ghormley, R. K., and Camp, J. D.: Osteogenesis Imperfecta, Radiology **40**:145-154 (Feb.) 1943.

20. Farber, J. E., and Margulis, A. E.: Blue Scleras, Brittle Bones and Deafness, Arch. Int. Med. **71**:658-665 (May) 1943.

21. Brailsford, J. F.: Osteogenesis Imperfecta, Brit. J. Radiol. **16**:129-136 (May) 1943.

22. Follis, R. H., and Jackson, D. A.: Renal Osteomalacia and Osteitis Fibrosa in Adults, Bull. Johns Hopkins Hosp. **72**:232-241 (April) 1943.

23. Soffer, L. J., and Cohn, C.: Primary and Secondary Hyperparathyroidism, Arch. Int. Med. **71**: 630-649 (May) 1943.

24. Curtis, L. E., and Feller, A. E.: Hyperparathyroidism with Calcinosis and Secondary to Renal Disease: Report of a Probable Case, Ann. Int. Med. **17**:1005-1014 (Dec.) 1942.

25. Orr, I. M.: Case of Parathyroid Adenoma, Brit. J. Surg. **30**:375-377 (April) 1943.

disappeared after parathyroidectomy and the blood chemistry became normal. Royde [26] tells of a similar case, in which death from hemiplegia prevented knowledge of the effect of the operation on the changes in the bones.

Gorham [27] stresses the differential diagnosis of hyperparathyroidism, with particular reference to Albright's syndrome, which is characterized by osteitis fibrosa cystica, brown pigmented spots on the skin and precocious puberty, particularly in females. The differential diagnosis is particularly important to avoid unnecessary operation on the parathyroid gland, as surgical treatment is futile in Albright's syndrome.

Osteopetrosis and Osteopoikilosis.—Several cases of osteopetrosis have been reported during the year, bringing the total to about 120. The case of Zimmermann [28] presents the usual roentgenographic findings of osteosclerosis and clinical manifestations of blindness and deafness, due to encroachment of the sclerotic bone on the cranial foramens. A previously unreported finding is diminution in the size of the auditory meati. Rosenthal and Erf [29] stress the differentiation of osteopetrosis and myelofibrosis from refractory types of anemia, splenomegaly and leukemia by sternal puncture and biopsy. Linsman and McMurray [30] present a case of fluoride osteosclerosis, which they feel is unique; but a number of cases of fluoride osteosclerosis have been previously reported.

Two cases of osteopoikilosis are reported. In 1 case, recorded by Horwitz,[31] the condition was discovered by chance on roentgen examination; in the other, recorded by Thompson, Hoover and Fulton,[32] it was found in a selectee who complained of pain in the joints. He was rejected for military service. Phalen and Ghormley [33] report a case of osteopathia condensans disseminata associated with coarctation of the aorta and discuss diminution of the blood supply as a possible cause, but they finally agree with others that all of the sclerosing osteopathies are probably due to some defect of the genetic arrangement, with faulty differentiation and growth of bone from mesenchyme.

Melorheostosis.—This condition was originally described by Leri and Joanny in 1922 and has characteristically been monomelic. Of the approximately 40 cases reported in the literature, that of Carpender and co-workers [34] is the only one in which both lower extremities were involved.

Calcinosis.—Inclan [35] reports 3 interesting and relatively rare cases of calcareous granuloma, characterized by the presence of a calcified tumor, with rapid and gigantic growth, which apparently in each instance arose from a bursa and involved surrounding muscle. The lesions were cured surgically. The author failed to determine the cause but believes this condition to be entirely different from calcinosis circumscripta.

Crushing Injury.—Bywaters [36] writes a thorough article on a condition which until recently has been little known. When first described, in 1941, by Beal and Bywaters, it was thought to be a new entity, but search of the literature revealed that it was described by German authors during World War I. The Medical Research Council in England has records of 70 cases.

The typical crushing injury results when a person is pinned by a limb beneath beams or pieces of masonry for several hours. When first removed he seems well, but he soon goes into shock. Protein-containing fluids help restoration of normal blood pressure, and the patient's condition seems better until the first or second urine passed is observed to contain blood and oliguria occurs. Meanwhile the limb swells and becomes hard and tense. Blisters are seen. Patchy anesthesia and varying degrees of paralysis are present. The patient continues in a state of mental apathy for about a week. The end of the first week is a critical period, for renal failure is characteristic. Diuresis occurs, and granular casts are seen in the urine. Death

26. Royde, C. A.: Case of Osteitis Fibrosa Cystica with Parathyroid Tumor, Brit. J. Surg. **30**:169-175 (Oct.) 1942.

27. Gorham, L. W.: Differential Diagnosis of Hyperparathyroidism with Especial Reference to Albright's Syndrome, New York State J. Med. **43**:415-418 (March 1) 1943.

28. Zimmermann, C. A. W.: Osteopetrosis (Albers-Schönberg Disease) with Case Report, Radiology **40**: 155-162 (Feb.) 1943.

29. Rosenthal, N., and Erf, L. A.: Clinical Observations on Osteopetrosis and Myelofibrosis, Arch. Int. Med. **71**:793-813 (June) 1943.

30. Linsman, J. F., and McMurray, C. A.: Fluoride Osteosclerosis from Drinking Water, Radiology **40**:474-484 (May) 1943.

31. Horwitz, M.: Osteopathia Condensans Disseminata (Osteopoikilosis), Radiology **40**:404-407 (April) 1943.

32. Thompson, R. H.; Hoover, R., and Fulton, H. F.: Osteopoikilosis, Am. J. Roentgenol. **49**:603-605 (May) 1943.

33. Phalen, G. S., and Ghormley, R. K.: Osteopathia Condensans Disseminata Associated with Coarctation of the Aorta, J. Bone & Joint Surg. **25**:693-700 (July) 1943.

34. Carpender, J. W. J.; Baker, D. R.; Perry, S. P., and Outland, T.: Melorheostosis: Report of a Bilateral Case, Am. J. Roentgenol. **49**:398-404 (March) 1943.

35. Inclan, A.: Tumoral Calcinosis, J. A. M. A. **121**:490-495 (Feb. 13) 1943.

36. Bywaters, E. G. L.: Crushing Injury, Brit. M. J. **2**:643-646 (Nov. 28) 1942.

occurs unexpectedly. In about one third of the 70 cases there was recovery. The prognosis is more favorable for a crushed arm than for a crushed leg.

The treatment as outlined by Bywaters consists first of administering alkaline fluid in amounts up to 3 liters a day, or enough to make the urine alkaline. Shock is treated with plasma, serum or blood, and local treatment is given to wounds and fractures. If the limb is viable, the author advises elevation, fascial incisions, administration of alcohol by mouth and local application of cold to the limb and heat to the body. If the limb is nonviable, amputation should be done early to prevent absorption of autolytic substances.

With the hope of explaining the pathogenesis of renal failure in "traumatic anuria" (crush syndrome), Corcoran, Taylor and Page [37] applied partially occluding tourniquets to the limbs of dogs for four hours and caused marked depression of renal function. They feel that renal vasoconstriction associated with the onset of shock explains the transient signs of renal irritation which may follow injury. Although it may play a part in the genesis of the syndrome, it alone does not reproduce this state.

Phosphatase in Diseases of Bone.—Jaffe and Bodansky [38] state that there are two large groups of phosphatase—acid and alkaline. According to these authors, alkaline phosphatase activity gives a rough indication of the severity and activity of Paget's disease and of rickets. In the latter, it not only is a good indicator of the severity of the condition but gives better information relative to the abolition of the rachitic state than does the calcium or the phosphorus content of the blood. The level of phosphatase and the severity of skeletal alterations, observed in roentgenograms, seem to parallel each other in hyperparathyroidism. From investigation it appears that the factor underlying the elevation is new formation of osseous tissue.

Muscle Hernias.—Two articles dealing with this condition have been published. Both deal with the condition as found in soldiers. McMaster [39] emphasizes the similarity of the small muscle hernia to varicosities on inspection. Most of the hernias are found on the anterolateral surface of the leg and are due to enlargement of a normal opening in the fascia for a nerve or blood vessel. The author reports 21 cases with 38 hernias in 1,800 admissions to an orthopedic clinic. Kitchin and Richmond [40] also report cases of hernia of muscle in soldiers.

Bursitis.—There seems to be an increased incidence of this condition with the accelerated work program. Schneider [41] has made an investigation of the trabeculae which are found in bursas and has revealed them to be composed of collagenous connective and adipose tissue, bone, fasciculi of skeletal muscle, arteries, veins and nerves.

Burgess [42] describes an interesting technic for the care of acute and chronic bursitis, in which a cataract knife is thrust into the bursa under local anesthesia and an incision then made through the bursal sac into the adjacent subcutaneous tissue. The fluid is pressed out into the soft tissues and a compression bandage applied. The author reports good results in 14 cases, with no loss of time from work. Buck, McDonald and Ghormley,[43] after examination of 270 specimens of bursas, obtained principally at operations for hallux valgus, conclude that adventitious bursas develop in fibrous connective tissue and are not present at birth. The process is one of mucoid and myxomatous degeneration rather than one of secretion.

Sudeck's Atrophy.—There has been a surprising interest in this condition, manifested by numerous reports. De Takáts and Miller [44] present an excellent article in which they conclude that the syndrome of Sudeck's atrophy is the result of a chronic stimulation of somatic and possibly of efferent vasodilator fibers. The reflex may soon subside, or it may become chronic and progressively increasing in its effects. Pain, localized and spreading, vasodilatation and osteoporosis characterize the fully developed syndrome, but the osteoporosis is a comparatively late manifestation. Emphasis is placed on early treatment, as progressively more radical methods are required later. The authors believe that the emotional status of the patient

37. Corcoran, A. C.; Taylor, R. D., and Page, I. H.: Immediate Effects on Renal Function of the Onset of Shock Due to Partially Occluding Limb Tourniquets, Ann. Surg. **118**:871-886 (Nov.) 1943.

38. Jaffe, H. L., and Bodansky, A.: Diagnostic Significance of Serum Alkaline and Acid Phosphatase Values, in Relation to Bone Disease, Bull. New York Acad. Med. **19**:831-848 (Dec.) 1943.

39. McMaster, P. E.: Muscle Hernia of the Leg, U. S. Nav. M. Bull. **41**:404-409 (March) 1943.

40. Kitchin, I. D., and Richmond, D. A.: Multiple Muscle Herniae, Brit. M. J. **1**:602-603 (May 15) 1943.

41. Schneider, C. L.: Trabeculae Traversing Human Bursae, Anat. Rec. **87**:151-163 (Oct.) 1943.

42. Burgess, E.: Treatment of Traumatic Bursitis by Internal Paracentesis, Am. J. Surg. **62**:165-168 (Nov.) 1943.

43. Buck, R. M.; McDonald, J. R., and Ghormley, R. K.: Adventitious Bursas, Arch. Surg. **47**:344-351 (Oct.) 1943.

44. de Takáts, G., and Miller, D. S.: Post-Traumatic Dystrophy of the Extremities: A Chronic Vasodilator Mechanism, Arch. Surg. **46**:469-479 (April) 1943.

aggravates symptoms. Treatment depends on the duration of symptoms and consists of repeated injections of procaine hydrochloride into the injured area, paravertebral sympathetic block, periarterial sympathectomy and sympathetic ganglionectomy.

Peripheral Vascular Disease.—Shumacker [45] emphasizes the beneficial effect of sympathectomy on obliterative arterial and vasospastic disease and the necessity of careful preoperative study to determine if the proposed sympathectomy will help materially. Excellent illustrations and text give an exceptionally clear description of dorsal and lumbar sympathectomy.

Homans [46] explains traumatic vasomotor spasm and the accompanying pain mechanism on the basis of a peculiar progressive and persistent reflex disorder involving the sensory nerves of the blood vessels, the spinal cord and the sympathetic system.

Hildenbrand [47] discusses the beneficial effects of physical therapy in the treatment of peripheral vascular disease.

45. Shumacker, H. B.: Sympathectomy in the Treatment of Peripheral Vascular Disease, Surgery **13**:1-26 (Jan.) 1943.

46. Homans, J.: Vasomotor and Other Reactions to Injuries and Venous Thrombosis, Am. J. M. Sc. **205**: 313-328 (March) 1943.

47. Hildenbrand, E. J. C.: Physical Therapy Measures in the Treatment of Peripheral Vascular Diseases, South. M. J. **36**:224-228 (March) 1943.

III. INFANTILE PARALYSIS

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Approximately three hundred articles on the various problems connected with poliomyelitis are listed in the *Quarterly Cumulative Index Medicus* for 1943. The majority of these are concerned with laboratory experiments with small animals, problems in epidemiology and transmission and physical therapy, owing to the stimulation of the work of Miss Kenny. A great many articles are repetitious. I have chosen only those reports which I felt would be most appropriate and interesting. It is obvious that space could not be allotted for fair abstracting of all the fine work described in the various scientific journals for the past year.

Causation, Transmission and Epidemiology.—Rosenow,[48] of the Mayo Clinic, holds the hypothesis that the causative agent of poliomyelitis is a pleomorphic streptococcus. He has consistently isolated a specific type of streptococcus from the stools of patients having epidemic poliomyelitis. Virus virulent for mice was obtained from stools, and the virus was produced with streptococci isolated from stools of patients in the acute stage of the disease. He suggests that the growth of streptococci in the gastrointestinal tract may be an important source of specific toxic products and of the virus in epidemic poliomyelitis.

Wesselhoeft [49] states that it is generally accepted by the members of the medical profession that a virus with peculiarities of its own is the etiologic agent in anterior poliomyelitis. Quoting Sabin and Armstrong, he says: "It is one of the smallest filterable viruses and is resistant to 1 per cent phenol and 15 per cent ether; furthermore, it is resistant to the usual degree of chlorination used to destroy enteric bacteria in drinking water. It is destroyed by oxidizing agents, such as hydrogen peroxide and potassium permanganate, by ultraviolet rays, and by heating to 55 C. or higher for 5 minutes." The virus is transmitted from person to person; this implies that man is the reservoir of the infection. Whether cotton rats and mice can harbor the human virus is one of the most recent topics of discussion. Experimentally the human virus is pathogenic for certain monkeys, and their susceptibility has made it possible to advance knowledge of the disease. Poliomyelitis is not a natural disease of the monkey, however, and observations for determining its mode of spread are limited to man himself. Apparently the portal of entry is the mouth. The virus leaves the body in the stools. Persons who have been in contact with patients with poliomyelitis have had the virus in their stools without showing any signs of the disease. During epidemics many persons who have been exposed by contact may show slight gastrointestinal disturbances and influenza-like maladies without involvement of the central nervous system. These findings are suggestive of a much wider spread of the infection than is indicated by the actual number of cases reported. The work of Aycock and Kramer confirms this conception, for it shows that immunity to poliomyelitis increases with age, as does immunity to other common infectious dis-

48. Rosenow, E. C.: Isolation of Specific Types of Streptococci and Virus from the Stool in Studies of Epidemic Poliomyelitis and Encephalitis and the Production of Virus from the "Poliomyelitic" Streptococci, Proc. Staff Meet., Mayo Clin. **18**:5-16 (Jan. 13) 1943.

49. Wesselhoeft, C.: New Conceptions of Acute Poliomyelitis, Bull. New England M. Center **5**:160-163 (Aug.) 1943.

eases. It is only when the central nervous system is involved that the disease can be recognized clinically.

Wyllie [50] presents modern views on the cause and early diagnosis and feels that the infective agent is a virus. There are several possible portals of entry. The early theory advanced by Flexner and Lewis, that the virus passes from the nasopharyngeal mucosa by way of the olfactory nerve to the olfactory centers, is receiving less support. The gastrointestinal tract as a portal of entry seems most likely. The fact that abrasions on the skin may be a possible portal of entry is based on the number of persons who acquire poliomyelitis after wading or swimming in virus-contaminated water. There is still considerable evidence that the oral pharynx is a possible site of invasion, since the average number of cases of infection following tonsillectomy is by far greater than the number of cases in which tonsillectomy is not done. Fairbrother and Hurst, according to Wyllie, feel that the virus spreads along the axons and not along the perineural lymphatics. The axons themselves are not damaged during the passage, but damage occurs at the ganglion cell stations. The rate of transmission along the axons is estimated to be 5.8 cm. a day. The virus can travel from the brain to the spinal cord, or vice versa. He recommends three weeks of quarantine.

Aisenberg and Grubb [51] were able to transmit poliomyelitis to a monkey by inoculation of a cavity in the pulp of a tooth. Pathologic changes characteristic of poliomyelitis were found in the gasserian ganglion and in many of the ganglion cells. This is only a preliminary report, and this possible route of invasion should receive further study.

Howe and Bodian,[52] in an effort to establish the existence of a pathway by which the virus invades the central nervous system from the gastrointestinal tract, fed a chimpanzee by stomach tube material infected with the human strain of the virus. On the fourth day, during the preparalytic stage, this animal was killed, and microscopic sections were made through different ganglions through representative levels of the entire spinal cord and through various abdominal viscera. All the tissue examined was normal except the celiac ganglion and the sympathetic chain of ganglions. These tissues showed histologic evidence of invasion by the virus. This experiment suggested to them that the inflammatory process was confined to the abdominal portions of the sympathetic nervous system, and therefore it seemed a likely pathway for invasion of the central nervous system from the gastrointestinal tract. [ED. NOTE.—These observations are not in agreement with those of Sabin,[53] who concludes that the visceral efferent pathway by way of collateral sympathetic ganglions, such as the celiac ganglion, is not a common route for progression of the virus from the intestine to the spinal cord. This conclusion is based on his ability to isolate the virus from the celiac plexus of only 1 of 8 patients examined, and in this 1 the paralysis was bulbar. The conclusions are further substantiated by failure to isolate the virus from the plexus of 5 orally infected monkeys.]

Jungeblut and Dalldorf,[54] in trying to determine the source of the virus of a small epidemic in New York, found a dead house mouse in the home of a person who had died of infantile paralysis. From this mouse they were able to isolate the virus, which produced flaccid paralysis in albino mice, cotton rats and hamsters. They also isolated from the brain stem of the dead patient a virus which was capable of inducing infantile paralysis in albino mice, cotton rats and hamsters. The two viruses were similar in that there was some neutralization with convalescent serum from patients involved in this epidemic.

Prior to 1940 Trask, Paul and Melnick [55] attempted to isolate poliomyelitis virus from flies, mosquitoes and other insects which were collected during eight epidemics, with negative results. In 1941, owing to improvement of methods and availability of the Java (cynomolgus) monkey, the workers in three laboratories (Paul; Sabin and Wood, and Toomey) reported the detection of virus in flies which were collected during the summer and fall of 1941 in areas of epidemics.

50. Wyllie, W. G.: Poliomyelitis—Modern Views of Etiology and Early Diagnosis, Practitioner **150:** 219-224 (April) 1943.

51. Aisenberg, M. S., and Grubb, T. C.: Poliomyelitis Induced by Inoculation of Tooth Pulp Cavities, J. Bact. **46:**311 (Sept.) 1943.

52. Howe, H. A., and Bodian, D.: A Note on the Penetration of Poliomyelitis Virus from the Gastrointestinal Tract in the Chimpanzee, J. Pediat. **21:**713-716 (Dec.) 1942.

53. Sabin, A. B.: Pathology and Pathogenesis of Human Poliomyelitis, J. A. M. A. **120:**506-511 (Oct. 17) 1942.

54. Jungeblut, C. W., and Dalldorf, G.: Epidemiological and Experimental Observations on the Possible Significance of Rodents in a Suburban Epidemic of Poliomyelitis, A. J. Pub. Health **33:**169-172 (Feb.) 1943.

55. Trask, J. D.; Paul, J. R., and Melnick, J. L.: The Detection of Poliomyelitis Virus in Flies Collected During Epidemics of Poliomyelitis: I. Methods, Results, and Types of Flies Involved, J. Exper. Med. **77:**531-544 (June) 1943.

The authors' method consisted of catching flies in traps which were baited with fish and placed outdoors near the house or privy. Flies were usually collected in six hours between 10 a. m. and 4 p. m. Biting insects were caught in nets. The flies were then preserved at a low temperature until ready for use. One to 600 flies were washed in 50 cc. of distilled water, and the same fluid was used to wash the inside of the container in which the flies were kept. This suspension was used for nasal instillation, while another portion, to which ether had been added (for bactericidal purposes), was used for intra-abdominal injection. Monkeys were inoculated intranasally on each of three successive days. Also 10 to 20 cc. of the suspension was given to each of the monkeys by one intra-abdominal injection. Poliomyelitis developed in 4 of the 39 monkeys, and the virus was isolated. All positive results were obtained with Java (cynomolgus) monkeys. All the suspensions used contained blow flies and greenbottle flies, but house flies were present in only 2 of the 4 specimens that elicited positive reactions.

In their second paper Trask and Paul [56] report on the clinical circumstances under which flies were collected. These were captured within areas of epidemics during and after the epidemics. Of 8 samples collected during epidemics, 4 yielded the virus. There was a potential (though not proved) source of virus (in the form of "exposed" human feces of recent origin) within a few yards or feet of four sites where flies were collected. Flies collected from three of these sites yielded the virus. The findings to date therefore merely indicate that under certain circumstances the virus is carried by flies and possibly their feeding habits may be responsible. The presence of the virus in these particular samples of flies could be entirely a resultant and not a causal factor in human poliomyelitis.

Bang and Glaser [57] carried out experiments with Theiler's mouse "poliomyelitis" virus and Lansing's mouse-adapted strain of human poliomyelitis virus, which showed that the virus may be recovered from an adult fly only when the adult itself is infected by feeding. Theiler's virus was recovered from the common house fly as long as twelve days after infection, but Lansing's virus survived only two days. These experiments were undertaken not to secure data on the transmission of human poliomyelitis by flies but to furnish a biologic background for further study.

The fact that the virus of poliomyelitis had been found in flies caused Power, Melnick and Bishop [58] to make a limited survey of the fly population within a given locality in the city of New Haven, Conn., in the summer of 1942. This was a nonepidemic year for poliomyelitis in this vicinity. This study was carried out over four months. Their conclusions were: (1) the total fly population reached its greatest size in July; (2) the common greenbottle fly was by far the dominant species of the summer; (3) the large bluebottle fly replaced the common greenbottle fly in dominance during the latter part of the summer. In no sample were they able to detect the virus of poliomyelitis.

Trask and Paul [59] isolated the virus from the stools of monkeys into which the virus had been introduced by intracutaneous inoculation. This was the first time that the virus had been recovered from the stools after this type of inoculation.

Maxcy,[60] after reviewing fifteen articles on water as a means of transmission of poliomyelitis virus, concludes that at the present time there is insufficient evidence to justify the belief that water is a medium of any practical importance in the spread of this disease and that its epidemiologic pattern differs from that of diseases known to be water borne.

Wenner and Casey,[61] during an epidemic of poliomyelitis in Alabama in the fall of 1942, made a study to determine the extent to which the population at large were carriers of the poliomyelitis virus during the epidemic. Stools from 176 of 181 persons were tested to determine the carrier rate in the adult and the juvenile population. The virus was found in the stools of only 3 children 2 to 6 years of age. None was found in adult stools. Though evidence of poliomyelitis was widespread in the population, only persons who were ill during the epidemic provided infective stools. The ease of detection of the virus diminished with decline of the epidemic. They

56. Trask, J. D., and Paul, J. R.: The Detection of Poliomyelitis Virus in Flies Collected During Epidemics of Poliomyelitis: II. Clinical Circumstances Under Which Flies Were Collected, J. Exper. Med. **77**:545-556 (June) 1943.

57. Bang, F. B., and Glaser, R. W.: The Persistence of Poliomyelitis Virus in Flies, Am. J. Hyg. **37**:320-324 (May) 1943.

58. Power, M. E.; Melnick, J. L., and Bishop, M. B.: A Study of the 1942 Fly Population of New Haven, Yale J. Biol. & Med. **15**:693-705 (May) 1943.

59. Trask, J. D., and Paul, J. R.: Intracutaneous Inoculation of Poliomyelitis Virus in Monkeys and Its Detection in Their Stools, Ann. Int. Med. **17**:975-978 (Dec.) 1942.

60. Maxcy, K. F.: Hypothetical Relationship of Water Supplies to Poliomyelitis, Am. J. Pub. Health **33**:41-45 (Jan.) 1943.

61. Wenner, H. A., and Casey, A. E.: A Community Study of Carriers in Epidemic Poliomyelitis, J. Clin. Investigation **22**:117-125 (Jan.) 1943.

concluded, therefore, that the virus does not remain active in the stools of most persons for more than a few weeks.

With the knowledge that neutralizing antibodies against poliomyelitis virus are not always found in the serum of patients immediately after they recover from the acute stage of the disease, Toomey [62] carried out some interesting experiments with horse serum which had been immunized with the virus of poliomyelitis. One experiment was carried out to determine whether horses which had been immunized could be kept immunized to a point where their blood serum would continue to show the same high titer of neutralizing antibodies. Twelve sets of neutralization tests were done. A titer of 1:250 was maintained for two years providing the horses were repeatedly inoculated with the "fortified" virus. Another experiment was carried out to determine whether the combination of virus and early specimens of serum, obtained a few weeks after the completion of immunization, would accelerate the production of poliomyelitis when injected intracerebrally into monkeys and whether if neutralizing antibodies were not found immediately after immunization they could be found at some subsequent date. Two horses were inoculated with a 10 per cent suspension of "fortified" antigen over several months. The first 9 specimens of serum obtained from 1 horse when given in combination with the virus accelerated the production of poliomyelitis in monkeys inoculated intracerebrally. Identical results were obtained with the first 3 specimens from the other horse. The antibodies were slow in developing and did not appear in the blood of the first horse until about one year after the beginning of immunization. The highest titer of antibodies, a titer of 1:250, was reached approximately fifteen months after the beginning of immunization and was still present twenty months after the beginning of immunization. He also found that the titer for the first horse dropped from 1:250 to 1:150 approximately two years after the beginning of immunization. By repeated injections of "fortified" antigen the animals in which the titer of antibodies had dropped from 1:250 to a lower titer could be reimmunized to a point where potent neutralizing antibodies could again be found in the blood serum. [ED. NOTE.—Further studies of this nature should be carried out, the results of which might shed some light on the now confused status of the use of human convalescent serum in the treatment of early poliomyelitis.]

62. Toomey, J. A.: Delayed Production of Poliomyelitis Antibodies, Am. J. Dis. Child. **66**:121-125 (Aug.) 1943.

Pathology.—Peers,[63] in studying lesions of the central nervous system during the convalescent period of poliomyelitis in man, shows the widespread invasion to which the central nervous system is subjected. A study was carried out on 3 patients, 1 of whom survived seven weeks, 1 fifteen weeks and 1 eighteen and a half weeks. The first 2 died of intercurrent infections. The cause of death of the third was not given, but it was not due to poliomyelitis.

From 2 of the patients the brain and the entire spinal cord, with most of the thoracic and lumbar root ganglions, the sympathetic chain and the gasserian and celiac ganglions, were removed. Microscopic examination showed that lesions in the cerebral cortex, consisting of perivascular collars of lymphoid cells and interstitial foci of microglia and astrocytes, were confined to the paracentral lobules. Some diminution in the number of Betz cells also appeared probable. Only minimal lesions were found in the basal ganglions and the thalami. In the midbrain the substantia nigra presented the most severe damage. Lesions in the pons were confined to the tegmentum. Loss of nerve cells was extensive in Deiters' nucleus and more patchy and asymmetric in the motor nuclei of the fifth and seventh nerves.

In the cerebellum lesions were found only in the tectal nuclei and in the cortex of the vermis. The most marked changes in the medulla consisted of cellular loss and scarring in the reticular substance similar to those seen in the pons. The spinal cord presented an almost complete loss of nerve cells throughout the entire length of the anterior horns of gray substance. In contrast, the lateral horns were comparatively spared. Patchy and asymmetric lesions were found in Clark's column. No changes appeared in the posterior horns.

In the white matter of the spinal cord there was a mild diffuse demyelination of most of the ventral and lateral columns with the exception of the pyramidal tracts.

A few small foci of lymphoid cells were found in the gasserian, dorsal root and sympathetic ganglions. Similar lesions were found in the meninges, but no lesions were found in the choroid plexus.

Dublin and Larson [64] made postmortem examinations in 12 cases of poliomyelitis, which revealed constant lymphoid hyperplasia of intestinal

63. Peers, J. H.: The Pathology of Convalescent Poliomyelitis in Man, Am. J. Path. **19**:673-695 (July) 1943.

64. Dublin, W. B., and Larson, C. P.: Pathological Findings in Poliomyelitis, Am. J. Clin. Path. **13**:15-17 (Jan.) 1943.

mucosa and mesenteric nodes. No lesions were found in the sensory ganglions or in the peripheral nerves, but the posterior horns of gray matter of the cord were involved. This involvement suggested to him an explanation of the painful stimuli which occur in poliomyelitis. In 1 case a second attack, which proved fatal, occurred four and a half months after the initial attack. Postmortem examination in this case revealed old (astrocytic gliosis) and new (lymphocytic and polymorphonuclear proliferations) cellular changes as evidence of infection with both attacks.

Carey [65] made a study of motor end plates and muscle fibers in monkeys inoculated with the Armstrong-Lansing strain of virus. Microscopic examination showed the disappearance of many motor end plates, which resulted in denervation at the myoneural junction, and the appearance of masses of inclusion bodies near the degenerated motor end plates. He also noted that the degeneration which began in the motor end plates proceeded in a centripetal direction in the axis-cylinders of many motor nerves. The rate of this degeneration was often unequal in the same muscle fiber.

Sabin [63] feels that recovery of a neuron only partially damaged by direct invasion of the virus accounts for the transitory paralysis in some cases. He states that the inflammatory reaction is the result rather than the cause of the neuronal damage. He made an excellent study of the pathologic features of poliomyelitis. He showed that although the primary lesion is in the anterior horn cells there is almost always some involvement of the posterior horns and the dorsal root ganglions of the spinal cord. He also demonstrated neuronal damage in the vestibular nuclei of the medulla, the roof nuclei and the vermis of the cerebellum and the motor cortex. The area of Brodmann of the precentral gyrus is described as "the center from which the impulses initiating voluntary movements on the opposite side of the body descend to the motor nuclei of the cerebrospinal nerves." The fibers of this area and fibers connecting this area with other subcortical regions are concerned with the correlation of postural and volitional motor control. [Ed. Note.—Sabin shows that this area is a frequent site of damage to the central nervous system. May not these features in part account for the incoordination and mental alienation about which one has heard so much recently?]

65. Carey, E. J.: Morphologic Effects of Poliomyelitis Virus upon Motor End Plates in the Monkey, Proc. Soc. Exper. Biol. & Med. **53**:3-5 (May) 1943.

Second Attacks of Poliomyelitis.—Nelson and Green [66] report that the Harvard Infantile Paralysis Commission found in a total of 6,000 cases 4 cases in which true second attacks of poliomyelitis had occurred. In all 4 cases the patients were under observation before, up to and subsequent to the time of the second attack. The histories and the clinical data of the 4 cases are cited. All diagnoses were established on the basis of the nature and the distribution of the paralysis. The attacks occurred under circumstances epidemiologically consistent with infantile paralysis. Segmental involvement of the spinal cord in each attack was different. They state that Fischer and Stillerman have made the only effort to determine the actual incidence of second attacks. Their estimation of the rate for second attacks was 3.4 per thousand new cases. This is somewhat higher than Nelson and Green's ratio, which was 0.66 per thousand. Available data suggested to them that the incidence of second attacks is approximately the same as that of recognized first attacks in the general population. This was not their definite conclusion, however. The average interval between attacks in their cases was five years, and the shortest was two years. They report that no accepted second attack reported in the literature has occurred in less than two years after the initial attack.

Dublin and Larson [64] report a second attack occurring four and a half months after the original attack. Postmortem examination revealed old healed lesions from the first attack and new lymphocytic and polymorphonuclear proliferation from the second and fatal attack. [Ed. Note.—I treated a patient with infantile paralysis beginning two months after the onset. This patient showed unmistakable calcaneovarus deformity with accompanying muscular weakness in the opposite foot, which followed an acute illness eight years previously. Clinically this was a second attack of the disease.]

Tonsillectomy and Poliomyelitis.—In an effort to explain the etiologic relationship between tonsillectomy and poliomyelitis, McCormick [67] states that it has long been recognized that lymphatic hypertrophy frequently is associated with poliomyelitis. The fact that other degenerative diseases of the central nervous system, including neurosyphilis, encephalitis, spinal sclerosis, beriberi and other conditions of vitamin B deficiency,

66. Nelson, N. B., and Green, W. T.: Second Attacks of Anterior Poliomyelitis: Report of Four Cases, Am. J. Dis. Child. **65**:757-762 (May) 1943.

67. McCormick, W. J.: Tonsillectomy and Poliomyelitis: A New Concept of Etiological Relationship, M. Rec. **156**:164-167 (March) 1943.

are accompanied by a somewhat similar lymphatic reaction indicated to him that generalized lymphatic hypertrophy is a response to the degeneration of nerve cells generally rather than a specific response to poliomyelitis. He also points out the relationship of lymphatic hypertrophy to vitamin B deficiencies. The author raises the question of the possible etiologic relationship of the basic constitutional condition of the patient which is responsible for the lymphatic involvement necessitating the tonsillectomy and the effect of the anesthesia from the standpoint of nutritional deficiency and anoxia. Comparative figures on the incidence in the 1937 outbreak in Toronto are cited.

Sabin [68] was unable to infect tonsillectomized monkeys by painting virus over the areas of operation.

Toomey and Krill [69] removed the tonsils from 6 monkeys and then flooded the denuded areas with a 10 per cent suspension of virus for five days, with negative results.

Francis,[70] in studying the factors involved in the infection of 5 children in one family with poliomyelitis soon after tonsillectomies, concluded that tonsillectomy serves to precipitate the severe disease in children who are apparently healthy carriers. The cases of these 5 children were reported by Toomey and Krill in 1941.

Pregnancy and Poliomyelitis.—Harmon and Hoyne [71] described the clinical course of two pregnancies, which adds further strength to the evidence that pregnancy has little influence on the course of poliomyelitis in the paralyzed mother, and conversely that in utero infection of the fetus occurs rarely, if at all. In both cases the mother survived and the convalescence from poliomyelitis was uneventful. In 1 instance the infant was stillborn. They were unable to isolate the virus from the spinal cord and concluded that death was produced by anoxia, because the mother had extreme respiratory difficulty and had to be placed in the respirator to sustain life during the height of the acute illness. The second baby was healthy, with no evidence of any paralysis at 10 months of age.

Diagnosis.—Rosenow [72] describes a cutaneous test for early diagnosis of poliomyelitis. This test is made by intradermal injection of 0.03 cc. of a 10 per cent solution of the euglobulin fraction of horse serum immunized to the streptococcus of poliomyelitis. The need for such a test is great, since specific changes in the spinal fluid are not always present for accurate diagnosis. Moreover, changes in the fluid do not occur until after penetration of the central nervous system by the infecting organism.

Rosenow [73] used this cutaneous test as a control for the size and number of therapeutic injections of poliomyelitis antistreptococcus serum necessary for best results. He concludes that the antigen, or toxin, is neutralized by the antistreptococcus serum and that the streptococcus is not a passive invader but a part of the infectious process in poliomyelitis now generally attributed to the virus. This human serum was first used in the treatment of the acute form of the disease in an epidemic in Davenport, Iowa, in 1917. The mortality rate in a series of 23 untreated patients was 35 per cent. In a series of 58 patients receiving the serum the mortality rate was 17.2 per cent. Seven patients of this group were practically moribund at the time of the first treatment. With these excluded, the death rate among the remaining 51 was only 5.9 per cent. There was often prompt disappearance or diminution of subjective symptoms, such as headache, pain in the affected extremity or extremities, restlessness and hyperesthesia or mental apathy; twitching or spasms of muscles, nausea and vomiting and diarrhea disappeared; reflexes that had been absent, unequal, diminished or increased became normal, or more nearly normal; lowering of the pulse rate, drop in temperature, usually after an initial short rise, and lessened rigidity of the neck or the spinal column were noted; there was no extension of progressive paralysis, and function of the muscles improved.

Jervis and Strassburger [74] describe a case of fatal poliomyelitis which was diagnosed clinically as infectious polyneuritis. The diagnosis of infectious polyneuritis was made on the basis of ab-

68. Sabin, A. B.: Experimental Poliomyelitis by the Tonsillopharyngeal Route with Special Reference to the Influence of Tonsillectomy on the Development of Bulbar Poliomyelitis, J. A. M. A. **111**:605-610 (Aug. 13) 1938.

69. Toomey, J. A., and Krill, C. E.: Tonsillectomy and Poliomyelitis, Ohio State M. J. **38**:653-655 (July) 1942.

70. Francis, T., Jr.: An Epidemiological Study of Poliomyelitis Following Tonsillectomy, Tr. A. Am. Physicians **57**:277-282, 1942.

71. Harmon, P. H., and Hoyne, A.: Poliomyelitis and Pregnancy, with Special Reference to the Failure of Fetal Infection, J. A. M. A. **123**:185-187 (Sept. 25) 1943.

72. Rosenow, E. C.: A Diagnostic Cutaneous Reaction in Acute Poliomyelitis, Proc. Staff Meet., Mayo Clin. **18**:118-128 (April 21) 1943.

73. Rosenow, E. C.: Studies on the Treatment of Epidemic and Experimental Poliomyelitis with Antistreptococcic Serum: Summary of Results, Proc. Staff Meet., Mayo Clin. **18**:403-408 (Oct. 20) 1943.

74. Jervis, G. A., and Strassburger, P. J.: Guillain-Barre Syndrome ("Infectious Polyneuritis") and Acute Anterior Poliomyelitis, Am. J. Dis. Child. **65**:431-439 (March) 1943.

normal spinal fluid, i. e., high total protein content and normal cell count, bilateral and symmetric distribution of muscular weakness, greater involvement in the proximal than in the distal portions of the extremities and the presence of optic neuritis. They stress the difficulty in differentiating between the two diseases and suggest that a large number of cases of the Guillain-Barré syndrome may be instances of poliomyelitis with a favorable outcome.

Early Treatment. — Toomey [75] inoculated 6 monkeys with Flexner's M. V. strain of poliomyelitis virus. Three were given 5 cc. of a 5 per cent solution of azosulfamide intravenously twice a day for seven days. All of the animals except 1 acquired quadriplegia at the same time. The one exception had been given azosulfamide. It became paralyzed a day earlier than the others. Sulfanilamide is the active component of azosulfamide. He thus concludes that this drug does not modify or prevent poliomyelitis in the Macaca mulatta monkey. [ED. NOTE.—The result of this experiment is in keeping with clinical results obtained with sulfonamide compounds in the treatment of other virus diseases.]

McCormick [76] compares the symptoms and the pathologic features of poliomyelitis with beriberi and other anoxic conditions and concludes that vitamin B deficiency may be a major etiologic factor in poliomyelitis. He believes that the pain and the spasm in muscles in poliomyelitis are due to anoxia of the tissues. Whereas the pain and the spasm are relieved by increasing the blood supply (by application of external heat, as recommended by Miss Kenny), the same results are obtained by a biochemical means, with vitamin B. Satisfactory results of this treatment in 4 cases are reported.

Toomey [77] treated a total of 9 patients with infra-red rays. Three of these patients had paralysis of the facial nerve due to poliomyelitis, and 6 had paralysis of the facial nerve due to peripheral neuritis. There was no movement in the muscles supplied by the facial nerve in the 3 patients with poliomyelitis prior to the treatment. Immediately after application of heat from infra-red rays they were able to move these muscles voluntarily for a few minutes. There was no movement in the muscles supplied by the facial nerve after application of heat from infra-red rays when paralysis was due to peripheral neuritis. He concludes from these observations that the patients with infantile paralysis must have had some fibers left connecting the facial muscles with the nucleus of the seventh nerve, since these muscles could be moved voluntarily after treatment. No movement would have been obtained had all cells of the nucleus of the seventh nerve been destroyed. This impressed on him the necessity of keeping the muscles in good condition, so that the nerve can have something to move when its function returns. He feels that this is best accomplished by some form of heat, which causes capillary dilatation and thus increases the flow of blood and results in improved metabolic activity of muscles.

Stone [78] reports on 11 patients who received artificial fever or artificial fever combined with intraspinal injections of thiamine hydrochloride. Six of the patients received artificial fever and vitamins B complex and E orally, and 5 patients received intraspinal injections of thiamine hydrochloride besides artificial fever and vitamins given orally. The children treated had extensive involvement of the musculature of one or more extremities associated with generalized pain and muscular spasm and rigidity of the neck and back. Three of the children had previously received hot fomentations for from two to six weeks, without relief of tenderness and pain in the muscles or improvement of the paralysis. The average course consisted of four treatments, although 1 child received seven artificial fever treatments and four intraspinal injections. The intraspinal injections of thiamine hydrochloride were given in doses of 20 to 50 mg. eighteen to twenty-four hours prior to the artificial fever therapy. After the first treatment the patients had some relief of spasm, pain had decreased and nursing care was much easier. After several treatments they appeared stronger, were able to sit up without support for the first time and exhibited a greater range of movement because of freedom from pain. The skin of the affected extremities had lost its dry, mottled appearance. The color of the skin and the temperature were normal, and the extremities appeared alike, although one was severely paralyzed. In those muscles which were not completely paralyzed there was an increase in strength at one or two points. No contractures developed. All movements of the joints could be carried out without discomfort, and no deformities of the back had been evidenced up to the time the report was written.

75. Toomey, J. A.: Poliomyelitis and Neoprontosil, Arch. Pediat. **60**:22-23 (Jan.) 1943.

76. McCormick, W. J.: The Mechanism of the Kenny Method and Its Correlation with Vitamin-B Therapy in Poliomyelitis, M. Rec. **155**:525-527 (Dec.) 1942.

77. Toomey, J. A.: Effect of Infrared Heat on Localized Poliomyelitis and Neuritis, J. Pediat. **22**: 135-141 (Feb.) 1943.

78. Stone, S.: Artificial Fever and Vitamin Therapy in Treatment of Anterior Poliomyelitis, Arch. Phys. Therapy **24**:350-361 (June) 1943.

The thiamine hydrochloride was administered for its nonspecific beneficial effect on metabolism of the nerve cells. The intraspinal route was preferable because it placed the thiamine in greatest concentration closest to the affected cells in the spinal cord and affected nerve roots. When it was administered twelve to eighteen hours before the next artificial fever treatment better diffusion of thiamine in the nervous system was assured.

The action of artificial fever was also nonspecific. It increased the rate of blood flow through the body and central nervous system. The saturation of the blood was augmented. Improvement in cellular metabolism was produced. Catabolic products were removed at a greater rate.

The vitamin E was given for its beneficial results in the treatment of fibrositis. The vitamin B complex was used because of its supposed synergistic action with vitamin E.

It is suggested that combined vitamin–artificial fever therapy has all the advantages of hot fomentations besides a favorable influence on the regeneration of some neurons not completely destroyed by the virus.

Kabat and Knapp [79] found that muscular rigidity and hyperirritable stretch reflexes in poliomyelitis disappeared temporarily during spinal anesthesia. On the other hand, intravenously administered pentothal sodium produced relatively little effect on spasm in muscles. These studies suggest that spasm may be the result of changes in the gray matter of the spinal cord due to invasion of the virus. They state that this view is corroborated by Schwartz and Bouman.[80] Kabat and Grenell,[81] in making a pathologic study of the spinal cord in human poliomyelitis, examined 78 patients who died in the acute stage of the disease. Inflammatory reactions about the internuncial neurons in the gray matter were noted in almost every case and constituted the most prominent pathologic change in most cases. Little or no injury to the anterior horn cells was observed in about 40 per cent of the cases, while in the other 60 per cent there was more or less destruction of large motor neurons. Since all impulses through reflex arcs as well as from higher centers, including the pyramidal tracts, must be relayed through the internuncial neurons to excite the large motor neurons in the anterior horn, they suggest that a lesion in these internuncial fibers should interfere with and disorganize synaptic transmissions to the anterior horn cells. This synaptic disorganization, which causes the removal of inhibition from the anterior horn cells, could account for the hypertonus and the incoordination. The effect of physostigmine and of neostigmine is to depress the function of an enzyme called cholinesterase. This enzyme is responsible for the rapid splitting of acetylcholine, rendering this powerful substance physiologically inactive. Thus neostigmine allows acetylcholine to accumulate to a greater extent than normal at synapses, parasympathetic nerve endings and myoneural junctions. With their pathologic observations and the effect of neostigmine as a basis, Kabat and Knapp [82] gave neostigmine methylsulfate or neostigmine bromide to a series of 24 patients who had had poliomyelitis from three weeks to seventeen months. It was necessary to give atropine sulfate along with the neostigmine except to patients under 6 years of age. For 20 of these patients the results were encouraging. Given with the Kenny method of treatment, the drug increased the range of passive motion, decreased or eliminated deformities in some instances by relaxation of hypertonus and in some cases improved active motion. In a majority of cases the drug appeared to accelerate recovery. In a number of cases the spasm was decreased more rapidly when given with the Kenny routine.

Galloway [83] cites 3 cases, in 2 of which life was undoubtedly saved by tracheotomy; in the third case life could perhaps have been saved had tracheotomy been performed ten minutes earlier. He points out that the normal secretion of saliva is from 1,000 to 1,500 cc. per day. This may be increased in certain nervous diseases. To this normal amount of secretion in anterior poliomyelitis may be added inflammatory nasal, pharyngeal and perhaps bronchial secretions. If this fluid cannot be completely expectorated, coughed out, swallowed or aspirated, it will gravitate to a level and obstruct the airway. This mechanical block produces anoxia, with a tendency to atelectasis and pneumonitis. If relief cannot be obtained by ordinary postural drainage and aspiration with the patient lying face down, tracheotomy followed by aspiration through the artificial opening is indicated. Use of the res-

79. Kabat, H., and Knapp, M. E.: The Mechanism of Muscle Spasm in Human Poliomyelitis, to be published.

80. Schwartz, R. P., and Bouman, H. D.: Muscle Spasm in the Acute Stage of Infantile Paralysis as Indicated by Recorded Action Current Potentials, J. A. M. A. **119**:923-926 (July 18) 1942.

81. Kabat, H., and Grenell, R. G.: The Pathology of the Spinal Cord in Human Poliomyelitis, to be published.

82. Kabat, H., and Knapp, M. E.: The Use of Prostigmine in the Treatment of Poliomyelitis, J. A. M. A. **122**:989-995 (Aug. 7) 1943.

83. Galloway, T. C.: Tracheotomy in Bulbar Poliomyelitis, J. A. M. A. **123**:1096-1097 (Dec. 25) 1943

pirator is no contraindication for tracheotomy, as a special device can be made to keep the rubber collar off the opening of the tracheotomy tube.

Experimental Studies for the Evaluation of Physical Therapy in Poliomyelitis.—Abramson, Flachs, Freiberg and Mirsky [84] measured the rate of blood flow during rest by the venous occlusion plethysmographic method in a series of 27 subjects with acute or chronic anterior poliomyelitis of one extremity. In the majority of cases the peripheral circulation in the involved extremity was the same as, and in some cases it was greater than, that in the opposite side. The cutaneous blood vessels in the affected extremity responded more markedly to the stimulus of cold than did those of the normal limb. This was shown by the excessive vasoconstriction on exposure to a low environmental temperature with an apparent decrease in cutaneous temperature. Those treatments which have previously been used to increase the blood flow through the affected parts should be reexamined for their therapeutic value.

Molander and Weinmann [85] made a study of 18 patients with poliomyelitis which developed in the summers of 1939 and 1942. Their study consisted of carrying the various joints through a short arc of motion (the range of motion extending to the point where resistance could be felt) in one group of patients and of carrying the joints through a full range of motion in the other group of patients. The rate of recovery was much greater in those for whom the joints were carried through the long arc of motion than in those for whom the joints were carried through the short arc. The full passive range of motion was reached much earlier with the "long arc" treatment, and with the "short arc" treatment the same range was reached much later and only after forced stretching and manipulation under anesthesia. Examination of the muscles showed that the recovery of muscular strength was in no way impaired by too much strain on the muscles stretched by the full range of motion. The authors' results show that use of the full unrestricted arc of movement causes no harm and, in fact, has certain advantages over use of the short restricted arc of movement.

In an effort to further elucidate the Kenny concept of muscular spasm, mental alienation and incoordination, Watkins, Brazier and Schwab [86] studied the electrical discharges of muscles while at rest, during passive stretching and during voluntary contraction, both in early and in late stages of poliomyelitis. Comparing these results with similar studies on normal controls and on patients with traumatic lesions of peripheral nerves leads them to conclude that the Kenny concepts of muscular involvement in poliomyelitis, although the basis of an excellent type of treatment, are inadequate as a physiologic explanation of the dysfunction present. In the acute stage only muscles with some degree of paralysis discharge electrical potentials while at rest. These abnormalities are not correlated with the presence of clinical spasm. Partially paralyzed muscles were found to be hyperirritable to passive stretching, indicated both by electrical discharges and by pain. The muscular tension thus developed appeared to be a reflex protective mechanism. The electrical activity in weak muscles at rest increased during the period of improving motor power, and results were analogous to those seen in muscles during regeneration of peripheral nerves. When the improvement in motor power ceased, spontaneous electrical discharges disappeared. No abnormal electrical activity is associated with a true muscular contraction, nor are any discharges present in completely paralyzed muscles. In their cases muscular weakness could not be attributed to mental alienation, since the subjective signs of the infective processes were always present in the paretic antagonists of muscles in spasm. Their studies uphold the use of the term "incoordination," but they feel that "disordered reciprocal innervation" is a more descriptive term for this type of dysfunction.

Moldaver [87] carried out an investigation on 49 patients to see whether or not the Kenny concept actually existed and, if present, whether these symptoms had been overlooked for more than a century. The "spasm" was studied by electromyograms and "mental alienation" chiefly by chronaxia. Chronaxia is a means of determining the degree of neuromuscular degeneration in a paralyzed muscle. He concludes that spasm in muscles is not the most damaging symptom of infantile paralysis and does not lead to neuromuscular degeneration. Spasm is not an entity but a complex phenomenon and results from the

84. Abramson, D. I.; Flachs, K.; Freiberg, J. A., and Mirsky, I. A.: Blood Flow in Extremities Affected by Anterior Poliomyelitis, Arch. Int. Med. **71**:391-396 (March) 1943.

85. Molander, C. O., and Weinmann, B.: Results of the "Long Arc" and the "Short Arc" Treatment in the After-Care of Poliomyelitis, Arch. Phys. Therapy **24**: 74-87 (Feb.) 1943.

86. Watkins, A. L.; Brazier, M. A. B., and Schwab, R. S.: Concepts of Muscle Dysfunction in Poliomyelitis, Based on Electromyographic Studies, J. A. M. A. **123**: 188-192 (Sept. 25) 1943.

87. Moldaver, J.: Physiopathologic Aspect of the Disorders of Muscles in Infantile Paralysis: Preliminary Report, J. A. M. A. **123**:74-77 (Sept. 11) 1943.

combination of the normal stretch reflex, meningeal irritation of the posterior roots, increase of normal tonus in healthy and strong muscles opposed to weaker paralyzed muscles and lesions of the dorsal root ganglion in the posterior horns. He states in his conclusions that in alienated muscles there is neither a functional paralysis nor a physiologic block. The partial or complete loss of the power to control is due to damage or destruction of anterior horn cells. He always found some degree of neuromuscular degeneration in the paralyzed muscles which were considered alienated. He further concludes that incoordination does not consist in a misdirection of nerve impulses but is caused, if at all, by the inability of partially or totally denervated muscles to respond to otherwise normal nerve impulses.

Kenny Method.—Miss Kenny,[88] in her article in the *Physiotherapy Review* for January-February 1943, uses the space allotted her not so much for discussing her concept of the disease as for presenting a review of her difficulties in the past and her beginnings in this country and for reporting the evidence that attempted to prove to the medical committee which visited her on Nov. 22 and 23, 1942 that her concept of the disease was correct.

Bennett[89] describes the Kenny concept of infantile paralysis and the Kenny method of treating the triad of symptoms.

He[90] points out the change in the original Kenny concept of the disease as published in 1937. He feels that the success of her method of treatment in Minneapolis must in no small part be credited to the able support of the medical profession working with her. He states that medicine owes a debt to Miss Kenny for her keen perception and devotion to the cause of treatment of poliomyelitis, which can be repaid only by an equally keen and devoted research designed to support or if necessary to intelligently alter that treatment which she and other serious investigators have introduced. To disagree on certain details of technic is a healthy attitude and a spur to continue research, but therapy must be based on sound, proved physiologic and pathologic effects as well as on brilliant results before it is right to say that it is the only treatment and that all others are wrong.

In discussing the influence of the Kenny concept of acute poliomyelitis on physical treatment throughout all stages of the disease Bennett[91] concludes:

> While the full acceptance of the Kenny concept is hampered by poor terminology and by our limited knowledge of many of the basic physiologic and pathologic facts responsible for the cause and the aftereffects of poliomyelitis, it is proving itself clinically sound. In the acute stage of the disease this concept presents a syndrome of clinical manifestations which may lead to widespread weakness and deformity unless immediately recognized and treated. No one of these clinical manifestations is new in the sense that it had never been seen before, but the full significance of the triad making up the syndrome had not previously been appreciated. It is evident that, since we had not been aware of the full significance of these clinical findings, our past forms of treatment are likely to be inadequate and must either be discarded or be modified in ways consistent with the new concept. We must not confuse the Kenny concept with the Kenny method. The Kenny concept is a presentation of clinical findings in the acute stage of the disease. The Kenny method is an attempt to treat these findings.
>
> In the convalescent stage the concept explains the cause of the development of contractural deformities and the spotty return of muscle power, and in this way indicates certain routines of treatment. These routines may be similar to those used in the past, but the reasons for their use may be quite different. In this stage there must be no temporizing in the face of beginning periarticular and intramuscular contractures. We have in the past learned how to deal with these contractures. We must not sit idle and hope that hot packs will dissolve the contractures in some magical manner. If they do not quickly respond to conservative measures they must be stretched out manually or even wedged out in plaster casts. We have long known the danger of allowing patients to bear weight and increase their activity unless correct structural alinement can be maintained. When the patient's activity should be increased and protective or supportive apparatus is indicated, such apparatus should be utilized as long as is necessary. Our statistical results may suffer but our patients won't.
>
> In the chronic phase of the disease the concept helps explain the results and perhaps points out the inadequacies of past treatment, but it solves the treatment problem in no way.

Bingham[92] gives a preliminary report on the treatment of a total of 60 patients with infantile paralysis at the Country Branch of the New York Orthopaedic Dispensary and Hospital. These patients were divided into three groups: (1) those having only Kenny treatment, (2) those

88. Kenny, E.: Kenny Concept of the Disease Infantile Paralysis, Physiotherapy Rev. **23**:3-7 (Jan.-Feb.) 1943.

89. Bennett, R. L.: Recent Developments in the Treatment of Poliomyelitis, South. M. J. **36**:152-156 (Feb.) 1943.

90. Bennett, R. L.: Basis for Physical Therapy in Acute Poliomyelitis, Virginia M. Monthly **70**:15-18 (Jan.) 1943.

91. Bennett, R. L.: The Influence of the Kenny Concept of Acute Poliomyelitis on the Physical Treatment Throughout All Stages of the Disease, Arch. Phys. Therapy **24**:453-460 (Aug.) 1943.

92. Bingham, R.: The Kenny Treatment for Infantile Paralysis: A Comparison of Results with Those of Older Methods of Treatment, J. Bone & Joint Surg. **25**:647-650 (July) 1943.

receiving Kenny treatment late in the course of their illness and (3) those having only the older methods of therapy. Follow-up studies were made three months later. He concludes:

> Patients receiving the Kenny treatment are more comfortable, have better general health and nutrition, are more receptive to muscle training, have a superior morale, require a shorter period of bed rest and hospital care, and seem to have less residual paralysis and deformity than patients treated by older conventional methods. The Kenny treatment is the method of choice for the acute stage of infantile paralysis.

[ED. NOTE.—I do not consider this a conclusive study, as three months is not a sufficient follow-up period in which to conclude that deformities will not occur.]

Northway [93] discusses his observations of Miss Kenny's method of treatment and not his experience with this treatment on a group of patients. He describes Miss Kenny's conception of muscular spasm, mental alienation, incoordination and treatment. His conclusions are:

> The Kenny method of treatment is most successful when used during the acute stage of the disease.
>
> Pain and muscle spasm are relieved and permanent contractures are prevented.
>
> Muscle tissue is kept in a physiological state receptive to muscle education and a return of function, provided anterior horn cells have not been permanently or too completely destroyed.
>
> Permanent paralysis is not prevented in the presence of massive anterior horn cell destruction.

O'Donoghue [94] feels that a great deal of criticism directed at the Kenny method of treatment is due to the method of presentation rather than to the material that has been presented. Sister Kenny's personality is a factor. He states that after considerable study and a minimum of observation the method appears to offer a definite improvement in the treatment of poliomyelitis. He is, however, equally convinced that with improper facilities and untrained personnel the Kenny method will do more harm than good and that without appreciation of this fact by the physician the method will rapidly fall into disrepute. He presents no comparative study.

Stuck and Loiselle,[95] in giving reports for the 1942 epidemic of poliomyelitis in San Antonio, Texas, report a total of 87 cases. The symptoms responsible for the diagnosis of poliomyelitis were fever, headache, stiff neck, stiff back and muscular weakness. Sixty-two patients had a paralytic type of the disease, while 25 had an abortive type and had no muscular weakness. All the patients who showed any muscular tenderness or weakness, stiffness of the back or hypertonus of muscles were given treatment as outlined by the Minneapolis group. Intensive treatment was abandoned only after all hyperirritability and pain of the muscles were overcome. Reexamination of all patients in January 1943 revealed that 30 patients were free from all effects of the disease, with no muscular weakness or hypertonus of any muscle group. These included the 25 who had an abortive type or only temporary weakness. Sixteen others had slight residual weakness. Twenty-nine had moderate to severe residual weakness. Six patients died, and results were unknown in 6 cases. Only 53 per cent of the patients, including those with the abortive type and those with only slight residual weakness, completely recovered. However, it is stated that follow-up examinations revealed more rapid recovery than usual among those who were not severely paralyzed at the onset, and indications were that there would be less residual deformity than usual.

Reporting on the first year of treatment at the Iowa Lutheran "Kenny Cottage," a pavilion of the hospital dedicated by Miss Kenny for the treatment of acute infantile paralysis during the contagious stage, Dyson [96] gives data on the results of treatment of 39 patients.

There was 1 death. Twenty-three patients remained in the hospital from one to two months; 10 remained in the hospital from three to five months; 5 were still in the hospital or remained there as long as seven months.

There were 25 complete recoveries; 3 patients had slight residual weakness and 10 marked residual weakness.

Patients who remained in the hospital two months or less made a complete recovery (with the exception of the 1 who died). Only 2 recoveries were reported for patients remaining more than two months. Three other patients, remaining three to five months, had slight residual weakness, and the remaining 10 had rather pronounced residual weakness. [ED. NOTE.—The important point is that in 23 of the 25 patients complete recovery took place within two months. Therefore only 2 of 25, or 8 per cent, needed treatment for longer than two months for complete recovery. It is apparent that most of the complete recoveries

93. Northway, W. H.: The Kenny Method of Treatment of Poliomyelitis, Stanford M. Bull. **1**:171-174 (Aug.) 1943.

94. O'Donoghue, D. H.: A Consideration of the Kenny Treatment of Infantile Paralysis, J. Oklahoma M. A. **36**:236-238 (June) 1943.

95. Stuck, W. G., and Loiselle, A. O.: The 1942 San Antonio Poliomyelitis Epidemic, J. A. M. A. **122**:853-855 (July 24) 1943.

96. Dyson, J. E.: The Kenny Treatment in Acute Poliomyelitis: A Report of the First Year at the Iowa Lutheran Kenny Cottage, J. Iowa M. Soc. **33**:375-379 (Aug.) 1943.

attributed to the method of treatment occurred in patients wih a nonparalytic form of the disease or in persons who would have made a spontaneous recovery.]

Toomey [97] presents an excellent article on the basic considerations needed for judging therapeutic results in infantile paralysis. An abstract of this entire article would be too extensive for this review. But his classification of patients, I think, is of sufficient interest to be quoted verbatim. He states that persons in whom the virus of poliomyelitis is present can be divided into nine groups:

Group 1. Those who have the virus in the gastrointestinal tract and who exhibit no symptoms. The number in this group will probably be great during epidemics.

Group 2. Those with virus in the gastrointestinal tract who merely have gastroenteritis (diarrhea or constipation), headache or some other nonspecific disturbance and no other symptoms.

Group 3. Those who have the aforementioned symptoms plus nausea and even pain in the belly. Groups 2 and 3 have what are termed abortive forms of the disease, and these patients too may be considered numerous.

Group 4. Those who have symptoms and significant changes in the spinal fluid but no paresis or paralysis.

Group 5. Those who in addition to the aforementioned symptoms have a positive Kernig sign (tightness of the muscles; hamstring tension of the posterior muscles of the hamstring group), a stiff back and no paresis or paralysis.

Group 6. Those who, in addition to a positive Kernig and a positive Brudzinski sign and a stiff back, have a stiff neck, some with marked opisthotonos. Groups 4, 5 and 6 are sometimes classified as "nonparalytic." They have no paresis or paralysis.

Group 7. Those who have all the previous signs and symptoms plus some segmental muscular paresis, which can be appreciated only on careful examination —a paresis not accompanied by any functional impairment or synchronous movement.

Patients in groups 2 to 7 inclusive arrive in a hospital for persons with contagious disease and usually recover within the isolation period of twenty-one days and are discharged cured. They rarely need to see an orthopedic surgeon; they rarely require any physical therapy other than that received in the hospital.

Group 8. Those who have all the signs and symptoms previously mentioned plus some obvious segmental weakness which does not fully approach paralysis and which does not interfere with synchronous rhythmic motion.

Group 9. Those who in addition to all the aforementioned signs and symptoms have a typical lower motor neuron lesion with segmental paralysis. Years ago it was rare that a patient got into a hospital unless he belonged to this group. At the present time, in communities which have become conscious of poliomyelitis conditions of diagnosis have so improved that in epidemics many patients with abortive, nonparalytic forms of the disease and patients with paresis belonging in groups 2 to 7 inclusive are recognized. They may constitute the majority of persons that are admitted to the hospital during an epidemic; in one of the epidemics in Cleveland they made up nearly 80 per cent of the patients, and in no epidemic have they constituted less than 30 per cent.

The patients in groups 8 and 9, those with paresis or paralysis, are admitted to the hospital and later cared for by the orthopedic surgeon and the physical therapeutist. In the future these will still be the only patients whom these specialists will see or in whom they will be interested.

Good results of any new therapy must be shown in the patients in groups 8 and 9. If other methods give equally good results and are less expensive they become the methods of choice. Patients within groups 1 to 7 inclusive who are given physical therapy during the period of isolation in the contagious disease hospital no doubt have an important bearing on the unusual recovery rate reported in recent epidemics. Toomey states that if one has 100 patients with infantile paralysis of whom 20 per cent are in groups 8 and 9 and 80 per cent in groups 2 to 7 inclusive, it is known that 80 will get well no matter what is done. If the entire group of 100 is treated, the recovery rate is 80 per cent to start with—a fictitious rate to attribute to any therapy.

Lenhard,[98] in reporting on the 1941 epidemic in Maryland, describes a study of 296 cases of poliomyelitis. Sixty-eight per cent of the patients made a complete recovery. Fourteen per cent had slight residual weakness. Only 2 per cent had complete disability. There were 9 deaths. Treatment consisted of protective care and physical therapy for weak muscles. There was no complete immobilization of the patients or of the extremities. There was usually continuous improvement of the muscles. As a rule, they did not remain unchanged for three or six months and then show increased power. Patients who did not recover rapidly or spontaneously needed prolonged treatment for recovery of maximum power in the weak muscles. Muscles do not improve in direct ratio to the degree of initial weakness. They may continue to improve for eighteen months in patients who are treated immediately after the onset of the disease. Patients seen later improve up to nine months.

Rechtman [99] describes in detail the "orthodox" system of treatment of infantile paralysis, particularly as carried out at the Betty Bacharach

97. Toomey, J. A.: Poliomyelitis: Basic Considerations Needed for Judging Therapeutic Results, Am. J. Dis. Child. **66**:635-651 (Dec.) 1943.

98. Lenhard, R. E.: The Results of Poliomyelitis in Baltimore, J. Bone & Joint Surg. **25**:132-141 (Jan.) 1943.

99. Rechtman, A. M.: Analysis of Treatment of Infantile Paralysis, with Comments on Kenny System, Arch. Phys. Therapy **24**:461-471 (Aug.) 1943.

Home. This method is the same or similar to generally accepted modes of treatment as practiced at the Georgia Warm Springs Foundation and in other places where a number of patients with infantile paralysis are admitted. It is the author's hope to make a comparison of the results of the study in the Betty Bacharach Home with the orthodox method of treatment and the results obtained with the treatment introduced by Sister Kenny. There is a general discussion on the Kenny method of treatment of infantile paralysis, which is a recapitulation of Miss Kenny's work. It is the author's impression that treatment of the acute phase of infantile paralysis will for the most part revert to the previous methods used at the Betty Bacharach Home and will incorporate those measures suggested by Miss Kenny that have proved of value. In either system, however, the final results depend on the expertness and the training of the person giving the treatment.

Key [100] compares the Kenny and the orthodox method of treatment of infantile paralysis. He discusses Miss Kenny's and the orthodox conception of spasm, incoordination and mental alienation. He concludes:

> The most important difference between the Kenny and the orthodox methods of treating poliomyelitis is that in the Kenny method emphasis is placed upon muscle spasm as the most important feature of the disease and efforts are made to relieve this spasm by hot fomentations, while in the orthodox method flaccid paralysis of muscles is considered the most important feature of the disease and efforts are made to protect and restore function to the paralyzed muscles. The other two symptoms which are stressed by Miss Kenny (incoordination and mental alienation) are recognized under different names, but are treated in much the same manner under each method. However, we believe that early active exercise of muscles is harmful and tends to prolong the stage of tenderness and contracture and we do not begin our muscle training until these symptoms have subsided, while Miss Kenny begins her muscle training as soon as possible after the diagnosis of poliomyelitis is made. We also consider splints a useful adjunct to our treatment where they are indicated.
>
> The symptoms which Miss Kenny calls muscle spasm are recognized and treated in the orthodox method, but they are called rigidity and muscle contracture and are treated by immobilization in splints or casts to relieve the pain and prevent contractures and the development of deformities. In anticipation of the criticism that even though orthodox treatment has recognized the so-called muscle spasm it has failed to emphasize and treat this symptom, I wish to state that rest is probably the most important therapeutic measure in our armamentarium and that in order to put a muscle at rest we immobilize the part. Consequently, we treat the tender, painful, contracting muscles by rest. This is obtained by our splints or casts. The reason we have not emphasized these symptoms is that they tend to subside when the limb is put at rest. The tendency of the muscles to contract (so-called muscle spasm) subsides when the pain and tenderness disappear and if deformities are prevented this symptom is rarely an important problem under orthodox treatment. It has not been emphasized because it subsides spontaneously.

Key [101] describes his conception of the standard treatment of infantile paralysis. He calls it an economical or common sense method and cites the under-water gymnasium of Lowman and the institute at Warm Springs and the prolonged protection of paralyzed muscles, combined with intensive physical therapy, as practiced by the Kendalls in Baltimore, as variations of the standard method. He cites twenty-eight reasons why the orthodox method described by him is superior to the Kenny treatment of poliomyelitis. He severely criticizes the statistics which show cures for 80 per cent of patients receiving the Kenny treatment as compared with 12 per cent receiving orthodox treatment, according to McCarroll's figures. The 80 per cent in the Kenny series include all the patients who make a spontaneous recovery. He declares that the proponents of the Kenny method do not recognize spontaneous recovery. The percentage cited by McCarroll include patients who had residual paralysis of sufficient degree to cause them to go to a hospital for treatment, and no temporarily paralyzed patients were included in the group.

Bohnengel [102] describes the Kenny concept of infantile paralysis and states that psychobiologic disorganization coexists with an anatomic-physiologic disorganization in acute infantile paralysis. He states:

> Although the Minneapolis group has never denied the occurrence of paralysis, they have, apparently under the influence of Miss Kenny, tended to minimize its importance in the clinical picture of infantile paralysis. This tendency undoubtedly arises from the realization that nothing is to be accomplished by treating a symptom which is the direct result of an irreversible structural lesion, whereas there is much to be gained by focusing attention on a reversible symptom which has proved amenable to treatment. The tendency, however, to minimize the importance of paralysis has been unfortunate. It has helped create a controversial situation in which much energy is being expended to prove on the one hand that paralysis and on the other that "mental alienation" is the disabling symptom, whereas the essential problem is to what extent each plays a role. Nevertheless, much new data have resulted from this controversy, and it is increasingly

100. Key, J. A.: The Kenny Versus the Orthodox Treatment of Anterior Polimoyelitis, Surgery **14**:20-31 (July) 1943.

101. Key, J. A.: Reasons Why the Orthodox Is Better Than the Kenny Treatment of Poliomyelitis, Surg., Gynec. & Obst. **77**:389-396 (Oct.) 1943.

102. Bohnengel, C.: Psychobiologic Factors in the Kenny Concept of Infantile Paralysis, Arch. Phys. Therapy **25**:350-356 (June) 1944.

apparent that the arguments are much more in agreement than are their respective proponents. Although there is sufficient well substantiated evidence that both symptoms do exist, there are many wide gaps in our knowledge of each.

The crux of the whole controversy over the Kenny concept lies in the fact that one group of observers, principally the Minneapolis group, is using psychobiologic methods of observation, experimentation and treatment and therefore brings into view only those of phenomena which exist at the psychobiologic level of organismic integration. The other group, using more purely physical methods of study, brings into its field of vision only those phenomena which exist at the anatomic-physiologic level of organismic integration. Both groups tend to lose sight of the fact that the two symptoms may be coexistent not only in the same individual but in the same muscle. It is important to subject the method of procedure to critical study before attempting an evaluation of the facts, a principle somewhat more rigidly adhered to in laboratory investigations than in clinical investigation.

Paralytic Scoliosis.—Farkas [103] gives an excellent description of the early clinical manifestations of paralytic scoliosis. He describes in detail the mechanical factors entering into the formation of the different curves. He states that a few weeks or months after the onset of infantile paralysis the spine discloses changes representing a pathologic entity—the paralytic spine. It is necessary to speak of paralytic spine instead of scoliotic spine since at the onset there is no lateral deviation; but the spine discloses significant features, as follows:

1. At the onset we observe enlargement of the intervertebral spaces, followed later on by dullness and cloudiness; the border lines between discs and vertebrae are effaced; and the spaces themselves become uneven and appear markedly narrowed. Ossification of the epiphyseal ring starts in some cases as early as the age of four; the process is very irregular, and the ossification is bulky and confluent. Minute or larger calcium deposits appear in the intervertebral spaces. This process may last for years, accompanied by general bone atrophy; in many cases after a couple of years the process apparently heals spontaneously.

2. Functionally, the paralytic spine is characterized by a high degree of flexibility and compressibility. Because of the increased mobility, univerteberal or segmental rotations appear first without any lateral deviation. Due to the flexibility, forward-backward tilting of one or more vertebrae occurs with the disappearance of thoracic kyphosis and lumbar lordosis. As a result of the increased mobility and compressibility—the prime factor in the formation of scoliosis—a translatory shift of the vertebrae appears.

The paralytic spine is the pathological condition preceding paralytic scoliosis. The scoliotic curve requires usually from four to five years before reaching its final form. Prior to this, the side of the convexity and the direction of the rotation may change several times. The rotation and compression of the spine are the chief factors in preparing the way for paralytic scoliosis.

The rotation is brought about by faulty mechanics of: (a) the pelvis (pelvic rotation); (b) the thorax and shoulder girdle (thoracic rotation); and (c) the respiration.

In pelvic rotation, all spinous processes point to the same side of the body. In thoracic rotation, the thoracic and the lumbar spinous processes point in opposite directions.

The cause of rotation is the pathological imbalance between the two sides of the body carrying out rotary motions of different degrees during the performance of the daily routine, especially during locomotion. The physiological imbalance, present in every human being, takes advantage of the decreased resistance of the rotary system of the spine—that is, damage of the discs—and causes the predominance of the right thoracic, left lumbar curves.

Paralytic scoliosis is brought about by the imbalance between the two sides of the body exerted on the paralytic spine. Paralytic scoliosis can be differentiated from scoliosis of any other etiology by the uniform density of the spine in the roentgenogram, by the excessive and early rotation of the vertebrae, and by the temporary concave rotation.

Curves resulting from pelvic rotation, except for the sitting curves, have a far better prognosis than the thoracic curves, especially if the latter are associated with respiratory disturbances.

Operations.—Girard [104] presents another method designed to lessen the disability brought about by fixed paralytic pelvic obliquity. In 3 cases he transplanted the origin of the hamstrings on the low side of the pelvis to the symphysis pubis. This transplant apparently lengthened the arm of the lever on which the adductors functioned and thereby increased their strength, necessary for better pelvic balance. He points out the importance of correcting the pelvic obliquity before attempts are made to correct the scoliosis of which the pelvis is a part. [ED. NOTE.—In true fixed paralytic pelvic obliquity no one operative procedure will fulfil all requirements necessary for restoration of anatomic alinement. There is always as much fixation above the pelvic level as there is below. In the majority of cases the abductors are contracted on the low side of the pelvis and the adductors and the lateral trunk group are contracted on the high side of the pelvis. In persons in whom this deformity has existed over a long period I do not believe it is possible to restore anatomic alinement by any operative procedures. There are too many widespread structural changes. These patients can be helped by improving the faulty distribution of weight of the superstructure. This can be accomplished by shifting the femoral shaft on the high side of the pelvis toward the midline by subtrochanteric osteotomy and shifting the femoral shaft on the low side of the pelvis in a lateral plane by subtrochanteric osteotomy. These

103. Farkas, A.: Paralytic Scoliosis, J. Bone & Joint Surg. **25**:581-612 (July) 1943.

104. Girard, P. M.: Paralytic Pelvic Obliquity: Transplantation of Origin of Hamstring Muscles to Symphysis Pubis, J. Bone & Joint Surg. **25**:169-176 (Jan.) 1943.

procedures do not in any sense correct the scoliosis and the obliquity of the pelvis, but they do enable the patient to walk with less effort and in a more orderly manner.]

Billig and van Harreveld [105] make a preliminary report on a new aspect of reinnervation of muscles, which heretofore has not been presented. This work is based on the fact that more than a normal amount of muscle can be innervated by a nerve by causing the motor axons to divide more extensively than they normally do and thus to innervate paretic muscle tissue. He states that a regeneration of nerve fibers in general is accompanied by branching. The first operation was on a 16 year old boy, who had a three year history of poliomyelitis, with residual drop foot on one side. It was carried out approximately two years prior to the time the article was written. The treatment consisted in crushing motor branches of the peroneal nerve. This was done with a Kelly clamp placed as close to the innervation as possible. This operation, of course, resulted in complete paralysis of the involved muscles until the time the motor axons had again grown out from the point of interruption and established contact with the muscle fibers. This regeneration required approximately two months. Immediately after the operation a short drop foot brace was applied, and no physical therapy was given. He states that at the present time the boy has full functional power in the leg and foot—that the atrophied muscles have regained their size so that external measurements of the leg's circumference closely approximate that of the unaffected leg. In 1 other case in which there was involvement of both lower extremities the femoral nerve was crushed as near the nerve as possible and the tibial nerve was crushed in the popliteal region. No physical therapy was given for three months. By this time the muscles had recovered more power than had been present prior to operation. The authors state that the patient has gained sufficient strength to walk correctly without a brace, which was necessary prior to operation. One hundred and two additional operations have been done, the data on which are not complete.

The open incision has been largely replaced by manual methods, in which the muscles are vigorously kneaded by smooth blunt instruments, particularly in the area where the motor axons enter the muscle. In the first patient on whom this was done the postoperative course approximated that for direct interruption of the axons. Nine months later his muscular power was slightly greater than that previous to the time of treatment. The advantage of manual pressure over actual crushing is that all the motor axons are not interrupted and temporary total paralysis does not result. It was estimated that the rate of reinnervation was 4 mm. a day.

105. Billig, H. E., and Van Harreveld, A.: A New Aspect of Muscle Reinnervation: A Preliminary Report, U. S. Nav. M. Bull. **41**:410-414 (March) 1943.

(To Be Continued)